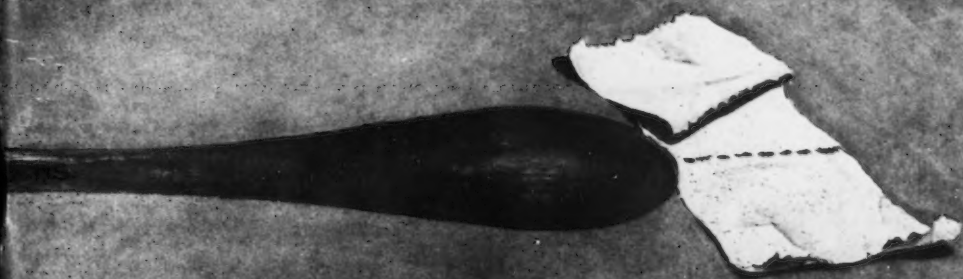


May 1954 Vol. 4 No. 3

Ca

a Bulletin of
Cancer Progress

Published by the
American Cancer Society, Inc.



Montana Division
American Cancer Society, Inc.
Billings, Montana

red herrings of cancer

One of the major obstacles to cancer control is the trivial nature of most of the early expressions of the disease. Too often, they are indistinguishable from a host of transitory complaints that many of us have experienced at some time or other and have safely ignored or treated expectantly. For example, blood in the stool is *USUALLY* due to hemorrhoids. The "lump" in the breast is *USUALLY* fibrocystic mastitis. Cough is *USUALLY* of inflammatory origin and *USUALLY* abetted by smoking.

The problem is further complicated by the fact that, as in the foregoing illustrations, complaints may in reality be due to obvious and benign causes, which, how-

ever, can and often do coexist with cancer. Thus hemorrhoids are encountered so frequently in patients with rectal cancer that they have been cited as symptoms thereof. Chronic cystic mastitis is so frequent a female phenomenon that it is bound to be found in many breasts also harboring cancer. Heavy smokers are apt to be coughers, yet a history of smoking can hardly be said to speak against the possibility of lung cancer in a man with a chronic cough.

The quality of mercy is prominent in the doctor, and therefore, faced with a choice between two explanations for his patient's complaint, the temptation to elect the happier one is strong. Yet when cancer is one possible explanation, that temptation must be resisted, regardless of the statistical probabilities. Digital and proctoscopic examination of the rectum in spite of hemorrhoids, frequent re-examination of breasts presenting adenofibrosis with insistence on biopsy of those in any doubt, and chest roentgenograms of all chronic coughers do disclose cancer often enough to make the thoughtful, careful doctor distrustful of the simple, the easy, and the readily "obvious."



Cover—

Blood in the stool—

CANCER until disproved

BLOODY MAN'S FINGER

A gentle reminder to do routine digital rectal examinations

NEWSLETTER

MAY, 1954

The Twenty-fifth Jubilee Anniversary of the founding of the Roscoe B. Jackson Memorial Laboratory at Bar Harbor, Maine, finds many old hands and new faces at Dr. C. C. Little's pioneering cancer research center.

Newest of all are the ideas and techniques now being employed to comb out of cancer the intricate relationships between genes, hormones, viruses, and aging. Emphasis continues to be placed on the virus-like agent, first reported here by Dr. John J. Bittner (now of the University of Minnesota), as the cause of mouse breast cancer. Subsequent work has shown that besides the agent (usually acquired from mothers in nursing), mice must have an inherited susceptibility and be hormonally disposed to develop this particular type of breast cancer.

Here is a rundown on current work at Bar Harbor:

Dickie and Lane have shown that mouse liver houses a great deal of the virus-like agent -- spleen little. Moreover, the active agent is found principally in liver-cell mitochondria (bundles of oxidative enzymes) and the lighter (supernatant) parts of spun-down liver tissues. Males, as well as females, carry the agent. As mice grow older, the agent loses its infective power -- or the mice lose the agent. These results are preliminary and may be modified by long-term observations.

Fekete finds that the milk factor is not influenced by embryonic environment. She transplanted to the uteri of cancer-resistant strains, fertilized ova of cancer-susceptible strains. Few developed breast cancer. As a matter of fact, about the same small percentage of mice developed cancer whether they were borne by their genetic cancer-susceptible mothers or by cancer-resistant foster mothers -- so long as they weren't nursed by mice with the agent.

Foster nursing of mice with low incidence of leukemia had no effect on the incidence of leukemia in a mouse strain susceptible to this disease. The incidence was high whether or not the mice were foster-nursed -- or whether or not they were borne by their own high leukemic mothers or a low leukemic female to whose uterus they were implanted.

Hummel has found that a rest (and lactation) between pregnancies halves the incidence of mouse breast cancer. Agentless but cancer-susceptible mice allowed to lactate had an incidence of 7 per cent breast cancer -- mice forced to breed again shortly after delivery had an incidence of 14 per cent.

These mice did not have the virus-like agent. If they had, the incidence would have been close to 90 per cent.

Stevens is investigating the reproductive potentiality of the ovary. He has found, surprisingly, that mice with only part of one ovary may be almost as prolific as mice with both ovaries intact. In the order of their reproductive capability were mice with: $\frac{1}{2}$ ovary, $\frac{1}{4}$ ovary and $\frac{1}{8}$ ovary.

Ovaries of old mice (approximately equivalent to seventy-five human years) gave rise to offspring when transplanted to young mice. There was a catch to this, however. The transplanted ovaries frequently developed tumors seven to nine months after transplantation.

Little and Hummel have raised grave doubts about the validity of a widely accepted hypothesis: that ovaries transplanted to the spleen and thus made to drain into the liver (where estrogens are destroyed and removed from circulation) become tumorous in response to overstimulation by the pituitary's gonadotropic hormones. They found tumors in ovaries merely transplanted from the ovarian capsule of one mouse to that of another. At this stage it appears that transplantation itself may bring about the tumors. Untransplanted ovaries do not become tumorous.

Dickie and Lane are investigating the combined effects of hybridization and castration in mice. What happens to the castrated hybrid offspring of two inbred strains of mice each showing a different response to castration? The hybrid female and male mice both show cancer of the adrenal cortex in all crosses. Some crosses show hormone-producing tumors of the anterior pituitary, and some, lung tumors. Some hybrid females show uterine abnormalities in the intact as well as castrated condition. Males in general resemble their sisters but are longer lived, and tumors of the adrenal and pituitary occur later in castrated males than in castrated females.

Runner is investigating pituitary and ovary interaction and the effect of this interaction upon mouse breast

(Continued after page 108)

C

a Bulletin
of
Cancer
Progress

Editor

Charles S. Cameron, M.D.

Executive Editor

William H. Stoner, M.D.

Assistant Editors

John F. W. King, M.D.

Brewster S. Miller, M.D.

E. Cuyler Hammond, Sc.D.

Mary C. Johnstone, B.Sc.

Mary Sullivan, B.A.

Patrick M. McGrady

Advisory Editors

L. T. Cuygeshall, M.D., *Chairman*

John S. Bouslog, M.D.

Paul E. Boyle, D.M.D.

G. V. Boudry, M.D.

R. Lee Clark, Jr., M.D.

Warren H. Cole, M.D.

Murray M. Copeland, M.D.

Frank S. Johns, M.D.

Raymond F. Kaiser, M.D.

L. W. Larson, M.D.

Mrs. Albert D. Lasker

William B. Lewis

Charles C. Lund, M.D.

Harry M. Nelson, M.D.

W. H. Parsons, M.D.

Alfred M. Pappas, M.D.

Elizabeth C. Stobo, R.N.

Howard C. Taylor, Jr., M.D.

Owen H. Wangensteen, M.D.

Art Consultant

Howard Sadayson

Circulation Manager

Russell Gray Smith

Please address all correspondence to
Charles S. Cameron, M.D., Editor
American Cancer Society, Inc.
47 Beaver St., New York 4, N. Y.

MAY 1954

VOL. 4, No. 3

CONTENTS

KEEPING UP WITH CANCER 74

AT A GLANCE 76

CANCER OF THE RECTUM: A REVIEW.

by J. W. McElwain, M.D.,

Harry E. Bacon, M.D., and

Howard D. Trimpi, M.D. 80

THE SECOND LOOK IN PATIENTS WITH
POSTOPERATIVE SYMPTOMS OF
CARCINOMA WITHOUT RECURRENCE,

by Calvin Reed Brown, M.D. 84

EXFOLIATIVE CYTOLOGY IN DISORDERS
OF THE COLON; A PRELIMINARY
REPORT, by Clarence C. Fuller,

M.D., Harold E. Clark, M.D.,

E. L. Hecht, M.D., and

Clifford Cohen, M.D. 86

PALPATION AND VISUALIZATION—
SIMPLE OFFICE PROCEDURES 90

ADENOMATOUS POLYPS OF THE
COLON AND RECTUM,

by Robert Turell, M.D. 92

THE MANAGEMENT OF MY
COLOSTOMY, by A

Colostomy Patient 97

CANCER OF THE STOMACH NEED NOT
BE FEARED, by Toyozo Nitta 99

CANCER CLINICS 101

DOCTORS DILEMMAS 105

NEW DEVELOPMENTS IN CANCER 107

Published bimonthly by

AMERICAN CANCER SOCIETY, INC.
New York, N. Y.

Annual Subscription \$2.50

Special bulk rate to organizations other than Divisions
subscribing in quantities of 200 or more.

Copyright, 1954, by the American Cancer Society, Inc.,
New York, N. Y.

Cancer "Sword" Reg. U.S. Pat. Off.



Keeping up

Au¹⁹⁸ in Treatment of Malignant Effusions

A simple technique for the intracavitary administration of Au¹⁹⁸ is described. In nine of twenty-four patients given this therapy, there was good clinical control of ascites and pleural effusions. Results indicate that intracavitary colloidal Au¹⁹⁸ is of distinct palliative value in selected cases. While there was evidence of radiation sickness and bone-marrow depression in some patients, these adverse effects were not severe. Except for the effect upon fluid accumulations, there was no evidence that this form of isotope treatment materially altered the course of disease in patients with advanced neoplasms. Although the effect of radiation on the superficial surfaces of neoplastic tissues lining the body cavities is important in controlling the fluid, it is not certain that the effect of radiogold on normal tissues is not important in producing the effect seen.

Andrews, G. A.; Root, S. W.; Kerman, H. D., and Bigelow, R. R.: Intracavitary colloidal radiogold in the treatment of effusions caused by malignant neoplasms. Ann. Surg. 137:375-381, March, 1953.

Diagnosis of Primary Hepatic Cancer

By careful evaluation of symptoms, signs, laboratory results, and hospital course, clinical diagnosis of primary hepatic cancer is possible. The most important symptoms are right upper-quadrant pain, anorexia, and weight loss. The commonest physical findings are ascites, jaundice, and hepatomegaly. Discrete nodularity of the liver is usually observed if ascites is absent. The liver is seldom tender. Spider angiomas, splenomegaly, and

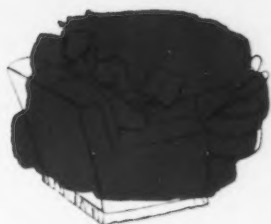
massive gastrointestinal hemorrhage may be seen. Hepatic tests are indicative of chronic and active hepatocellular damage but not of the cause of damage. Positive cephalin flocculation and thymol turbidity reactions early in the course signify active hepatocellular change. Zinc sulfate flocculation and gamma-globulin turbidity are more sensitive indicators than reversal of the albumin: globulin ratio. The alkaline-phosphatase level is not considered to be of much differential value. Red and white blood counts and urinalysis are usually normal. The rapidly downhill course helps to differentiate carcinoma from cirrhosis. Objective confirmation of the diagnosis can be made by needle biopsy of the liver or exploratory laparotomy with direct biopsy.

Galluzzi, N. J.; Weingarten, W.; Regan, F. D., and Doerner, A. A.: Evaluation of hepatic tests and clinical findings in primary hepatic cancer. J. A. M. A. 152:15-16, May 2, 1953.

Cancer of the Bladder

The results five years or longer after simple cystectomy in forty-nine cases of infiltrating cancer have been compared with those obtained by segmental resection in a similar group of forty-six cases. Cystectomy provided a somewhat higher survival rate than segmental resection when the tumor was deeply infiltrating and a somewhat lower survival rate when it was superficially infiltrating, regardless of its cellular appearance. Urological complications, usually renal, could be demonstrated in nearly all patients five years after ureterointestinal anastomosis. In the cystectomy series the survival rate remains about 50 per cent each year after

with Cancer



the fifth for as long as nine years. The survival rate following segmental resection is much better, and two of three patients with infiltrating cancer are apparently well after eleven years. Resection, however, is usually not the procedure of choice when the tumor has a very large circumference or poorly defined margins or when it lies close to the vesical orifice in the female patient. Proof of the superiority of radical cystectomy, with or without exenteration, will depend largely on the results five years or more after operation in cases with microscopic evidence of metastases in the lymph nodes.

Jewett, H. J.: Simple cystectomy and segmental resection for cancer of the bladder. J. Urol. 70:620-623, Oct., 1953.

Retroperitoneal Tumors

The literature concerning large retroperitoneal lipomatous tumors is reviewed. These neoplasms, often called lipomas, are deceptively benign originally, both in macroscopic and microscopic appearance, but they tend to recur and often end as full-fledged malignant tumors. It is recommended that any mass in the abdomen, especially if it is large and displaces abdominal organs, should be explored. Of the cases reported in the literature, sarcomatous change has been found in 47 per cent. The most frequent patient age was from 40 to 60 years, and the sex ratio was one male to two females. These tumors are characterized by prodigious growth and increasing tendency to malignant transformation, although some portions of the tumor remain entirely benign. The lesions show a peculiar arrangement of connective tissue in the form of

stalks, which is uncommon in ordinary lipomas. These tumors recur very slowly and, as a rule, do not metastasize. They should be removed as early and as completely as possible, thus giving the best chance of long survival if not of cure. They kill by compression of vital organs.

Noehren, A. H.; Goembel, T. E., and Tannhauser, S.: So-called retroperitoneal lipoma. Ann. Surg. 138: 779-783, Nov., 1953.

Gastric Ulcer and Gastric Cancer

A review of the records of all patients operated on at the Portland [Oregon] Clinic for gastric ulcer and gastric cancer during the six years from 1946 to 1952 confirms the fact that in a high percentage of cases benign and malignant ulcers are indistinguishable either preoperatively or at operation. During this interval seventy patients with gastric ulcer were operated on. Of the pathological examinations made in sixty-six cases, eight of these lesions were found to be malignant. During the same period seventy-four were operated on in the Portland Clinic for carcinoma of the stomach. These include the eight with malignant ulcers. Twenty-four lesions were inoperable. For the ulcer proving to be malignant, the common surgical procedure for gastric ulcer of removing the lower two thirds of the stomach is entirely inadequate. To circumvent this possibility radical subtotal gastrectomy is advocated for all gastric ulcers. There has been no increase in operative mortality resulting from such extension of simple ulcer resections.

Boyd, A. M.: Radical gastrectomy for benign gastric ulcer. Surg., Gynec. & Obst. 97:151-158, Aug., 1953.



a glance . . .

one-minute abstracts
of the current literature
on cancer . . .

Carcinoma of the Rectum and Colon

The concept of treatment of the geriatric patient with carcinoma of the colon and rectum has undergone a significant change. Now physiological, not chronological, age is a deciding factor in determining whether a patient can submit to major surgery of the colon or rectum. A series of 100 consecutive major operative procedures on the colon and rectum performed before 1941, and since 1951, are compared. This series shows that it is possible to perform major surgery of the colon and rectum in an older age group (an average of five years older) with a definitely lowered operative mortality. This is due to the use of antibiotics and to physiological control of fluid and electrolytes in the preoperative and postoperative periods. It is important to evaluate adequately the cardiac, nutritional, and general physiological level prior to surgery. The diagnostic significance of blood in the stool is emphasized and until proved otherwise should be assumed to be from carcinoma. Digital examination of the anus and rectum will lead to the diagnosis in 60 per cent of all carcinomas; sigmoidoscopic examination will give similar results in 80 to 90 per cent of all

carcinomas of the large intestine. Sigmoidoscopic examination is the only means of diagnosing lesions high in the rectum and in the lower sigmoid, for roentgenography in this area is entirely inadequate.

Campbell, F. B., and Samson, R. B.: Carcinoma of the colon and rectum in geriatrics. J. Am. Geriatr. Soc. 1:557-560, Aug., 1953.

Detection of Colonic and Rectal Polyps

The program of polyp detection developed at the Carle Clinic during a period of twenty-four months revealed fourteen cases of early and curable cancer of the colon during the course of 4851 visual and roentgenographic examinations. Under the adopted scheme, most adult patients undergoing general work-up received a roentgen-ray study of the colon by means of high-voltage radiography. Radiolucent objects are visible as negative shadows when the density of the barium mixture required for this high-voltage technique is properly balanced against the voltage. Rectoscopy (proctoscopy limited to the rectum) is performed on adult patients without definite symptoms in the X-ray Department and does not interfere with the roentgen-ray examination of the colon. It is concluded

that the routine use of the proctoscope by the general practitioner should lead to the discovery of polyps in from 8 to 10 per cent of adult patients. Because of their malignant potentialities, early detection and treatment of polyps of the colon and rectum will prevent the development of a substantial number of cancers of the large intestine.

Gianturco, C., and Miller, G. A.: Program for the detection of colonic and rectal polyps. J. A. M. A. 153:1429-1430, Dec. 19, 1953.

Advanced Carcinoma of the Colon and Rectum

Advanced carcinoma of colon and rectum is not necessarily inoperable because of extension into adjoining tissues. If distant intra-abdominal metastasis has not occurred, exploratory dissection of a neoplastic mass may demonstrate the resectability of the primary lesion with the involved adjacent structure for an additional 9 per cent of patients. The common sites of extension are the parietal peritoneum, abdominal wall, fallopian tubes, uterus, urinary bladder, duodenum, pancreas, stomach, spleen, and diaphragm. The analyses of data presented indicate that the best results were obtained in patients with primary carcinoma of the rectum infiltrating the body of the uterus. The patients with a neoplastic process infiltrating into the abdominal wall or perineum had the poorest results. The operative excision included the entire neoplastic mass removed en bloc. Removal in continuity was not possible when partial excision of the liver was required.

Van Prohaska, J.; Goyottis, M. C., and Wasick, M.: Multiple organ resection for advanced carcinoma of the colon and rectum. Surg., Gynec. & Obst. 97:177-182, Aug., 1953.

Colostomy Irrigation Apparatus

Protracted and unpleasant colostomy irrigation is unnecessary and can be avoided by using an apparatus that is simple, inexpensive, and efficient. The basic elements of the apparatus include a Paragon colostomy disk and belt, a long, pliable, open-end tube of latex rubber with

a side arm, and a urethral catheter passed through an infant's bottle nipple. The central portion of the colostomy disk is cut out to conform to the colostomy, the disk being held to the body by the belt. Irrigation is done in the sitting position by insertion of the catheter and nipple through the side arm. When the proper amount of fluid has been injected, the catheter and nipple are either kept in place temporarily to prevent too rapid expulsion of the fluid or removed immediately, depending on the characteristic action of the colostomy. A rubber band is used to close the side arm when the catheter is removed. The fluid drains into the toilet bowl through the long tube. If expulsion of the fluid is delayed or if the expulsion continues over a prolonged period, as usually happens, the end of the tube is closed with a rubber band or a broad, screw-type clamp. In this manner, the patient may carry out other activities while awaiting completion of expulsion. Most patients employ 2 irrigations of 1 liter each and require about forty-five minutes for the entire process. With this apparatus, two thirds of the period can be devoted to activities other than care of the colostomy.

Hurwitz, A., and Alderman, D. B.: An original apparatus for colostomy irrigation. New England J. Med. 249:410-411, Sept. 3, 1953.

Polyps of the Colon and Rectum

Polyps of the colon and rectum occur frequently and are true tumors and forerunners of one of the most common forms of cancer. Of great significance is the fact that a high percentage of malignant lesions of the colon and rectum originate in a pre-existing benign mucosal polyp that, in most cases, can be removed or destroyed with relative ease. An extensive statistical survey of 400 patients treated between 1945 and 1950 has just been completed at the Lahey Clinic with the following pathological findings: benign mucosal polyps, 218 cases; benign mucosal polyps with early carcinoma, 38 cases; and no pathological change, 151 cases. Benign mucosal polyps were associated with carcinoma of the rectum in fifty patients and

with carcinoma of the colon in nineteen. It is the policy at the Clinic to include a digital examination of the rectum and a sigmoidoscopic examination on all patients who report for a complete physical examination, the absence of such classic symptoms as rectal bleeding, alterations in bowel function, or unexplained abdominal pain notwithstanding. The increase in the number of benign polyps detected in patients has been in direct proportion to the number of sigmoidoscopic examinations performed regardless of symptomatology. Fulguration with high-frequency unit of all small, obviously benign adenomatous polyps that are easily reached with the sigmoidoscope and are below the peritoneal reflection is accomplished without biopsy. Radical resection is recommended if invasive cancer is found and there is any suggestion that it may have spread beyond the pedicle of the polyp.

Swinton, N. W., and Doane, W. A.: *The significance and treatment of polyps of the colon and rectum.* New England J. Med. 249:673-678, Oct. 22, 1953.

Reaction to Antibiotics Simulating Rectal Cancer

Reports in the current medical literature concerning untoward reactions to antibiotics have described anorectal manifestations ranging from pruritus ani to massive loss of blood, as well as changes in the rectal mucosa varying from edema to ulceration. A case of a 61-year-old white man referred because of uncontrolled rectal bleeding in January, 1952, is presented. Its outstanding feature was delayed onset of bleeding after diarrhea had immediately followed the use of antibiotics approximately six months earlier. Proctoscopy revealed an annular lesion, 8 cm. above the anal verge, that bled freely wherever touched although no ulceration was visible. The clinical impression was carcinoma of the rectum. Part of the principal lesion and a small polyp-like growth were removed for biopsy examination. The report on the biopsy was "inflammatory polyp of the rectum." Therapy was based on the hypothesis of

an allergic or possibly toxic reaction to antibiotics. Despite negative stool findings a topical overgrowth of *Monilia* was not entirely ruled out, and the lesion was painted with a 2 per cent aqueous gentian-violet solution through the proctoscope. There was favorable response to antiallergic and anti-*Monilia* therapy and proctosigmoidoscopy showed normal rectal mucosa.

Vogel, F.: *Delayed inflammatory reaction to antibiotics simulating carcinoma of the rectum.* New York State J. Med. 53:3037-3038, Dec. 15, 1953.

Carcinoma of the Rectum and Anus

Many cases of cancer of the rectum are amenable to cure until the very late stages of the disease and every effort should be made to improve present results. Tumors of the upper rectum have a better prognosis than the low lesions in which more extensive involvement is present. A surgical procedure is described for the excision of low-lying cancers of the rectum—those located below the middle valve of Houston. This operation is also indicated for carcinoma of the anus and extensive lesions of the upper rectum with invasion of the uterus or bladder. It should not be performed as a palliative procedure and is contraindicated when the general condition of the patient is poor. Although the operation described is still in the experimental stage, results obtained thus far seem to justify further trial. It has been performed in thirty-two cases, both for low- and for high-lying lesions.

Sauer, I., and Bacon, H. E.: *A new approach for excision of carcinoma of the lower portion of the rectum and anal canal.* Surg., Gynec. & Obst. 95: 229-242, Aug., 1952.

Proctosigmoidoscopy for the G. P.

The author estimates that 75 per cent of malignant neoplasms of the large bowel have adenomatous backgrounds. Practically all patients presenting themselves with any type of anorectal symptoms immediately make a self-diagnosis of piles. Fifteen per cent of a very large group of patients with rectal bleeding were found to have one or more adenomas. Adenomas

are easily found and should be destroyed as precancerous. Many doctors feel they have made a thorough examination when they have searched for evidence of hemorrhoids, fissure, and perhaps a low-lying epithelioma; this, however, does not preclude the presence of a small adenoma hidden in the rectum, which can only be found by proctoscopy. Emphasis is placed on the importance of thorough training of interns in proctoscopic pathology and methods of examination. The proctoscope is an important diagnostic instrument that should be in every practitioner's handbag.

Bowman, F. B.: Proctosigmoidoscopy for the family physician. Canad. M. A. J. 68:244-245, March, 1953.

Diagnosis of Carcinoma of the Colon

Approximately two thirds of the cases of carcinoma of the colon are incurable when the patient is hospitalized. Better results may be achieved by: (1) excision of known precancerous lesions, (2) more frequent use of the sigmoidoscope, and (3) routine rectal examination. All polyps should be removed unless the procedure is impossible because of other disease. If familial polyposis is found, total colectomy should be done. The procedure is also advisable for patients with ulcerative colitis who have pseudopolyposis and irreversible fibrotic changes in the wall of the colon.

Paine, J. R.: Early diagnosis of carcinoma of the gastro-intestinal tract. J. Indiana M. A. 46:737-744, Aug., 1953.

Carcinoma of the Rectum and Colon

A review of 461 necropsy cases of carcinoma of the colon and rectum at the Cook County Hospital is presented. In the series of 134 cases of carcinoma of the rectum (29 per cent of the total series

reported), 70.5 per cent of the patients were men and 29.5 per cent were women. In the remaining 327 cases of carcinoma of the colon there was an incidence of 59.3 per cent in men and 40.7 in women. Metastases to the liver, the most frequent site of metastases for both carcinoma of the colon and of the rectum, occurred in 39 per cent of carcinomas of the colon and in 36 per cent of carcinomas of the rectum. Far distant lymph-node metastases, as well as visceral metastases, may occur without regional lymph-node involvement as metastases to a main or intermediate lymph node near the origin of one of the main vessels. Venous emboli may also explain far distant visceral metastases without local involvement. The most important two signs and symptoms that brought the patient to the hospital were pain and rectal bleeding. The pain was almost invariably described as colicky and was associated with either complete or incomplete obstruction. There was evidence of obstruction in 208 patients, 46 per cent of all cases of carcinoma of the colon and rectum. Change in bowel habits was observed more frequently in the right half of the colon and was one of the presenting complaints in 60.5 per cent of the total series. The reason for the better prognosis for lesions of the right side than for lesions of the left side of the colon can be accounted for on the basis of: a higher incidence of left-sided annular constricting carcinomas associated with more extensive metastases, a higher rate of recurrence of carcinoma of the sigmoid and rectum, and higher resectability of the lesions of the right side of the colon. That the course of symptoms is determined by the location of the primary tumor and by the pathological character of its growth is clearly demonstrated.

Ascherman, S. W.: Carcinoma of the colon and rectum: review of four-hundred sixty-one necropsy cases at Cook County Hospital from 1929 to 1952. A. M. A. Arch. Surg. 66:208-217, Feb., 1953.

Cancer of the Rectum: A Review

*J. W. McElwain, M.D., Harry E. Bacon, M.D.,
and Howard D. Trimpi, M.D.*

Killer

In 1949 there were 10,309 deaths in the United States from cancer of the rectum.² This figure represents 5.5 per cent of all deaths from neoplastic diseases and therefore is of statistical importance. Despite better diagnostic procedures and a keener awareness of this disease by both the physician and the laity, the yearly number of deaths owing to cancer of the rectum continues to mount. In 1940, for example, only 8860 deaths were due to it. Although this increment can be explained partly by population increase and partly by the increase in average longevity, there still exists an actual, mounting mortality from cancer of the rectum on a corrected, statistical basis.

Ten per cent of patients admitted to surgery present gross liver metastases, and today it is the opinion among surgeons that hope for five-year survival is limited to less than 50 per cent of all cases. However, it is our opinion that at least 75 per cent could be given a chance for cure through earlier diagnosis and close adherence to the principles of adequate radical surgery.

Exactly what can we do? Until a cure for cancer is discovered and its prevention assured, we can continue to educate the layman and keep the physician well informed on scientific advancements in the diagnosis and treatment of this grievous condition.

Rectal cancer occurs in 60 per cent of men and 40 per cent of women, and is most likely to appear in the 50 to 60 year age group. There is no race or color predisposition.

The Patient

The patient must be taught not to disregard any aberration of bowel function

that cannot be explained feasibly by a transient intestinal illness. Change in bowel habit is of tantamount importance. Whether the patient develops constipation, diarrhea, mucus in his stools, or a change in frequency, caliber, or amount of stool, he must be educated to consult his family doctor. Too often bleeding is attributed to hemorrhoids, pain to anorectal infection, and the continual urge to defecate to dietary indiscretions and bowel stasis. Other symptoms that a patient may exhibit are a feeling of incomplete evacuation following bowel movements and a sensation of pressure in the pelvis. There is no table of symptoms that can be constructed to separate an early from a late lesion, but in general the early tumors tend to manifest themselves by bleeding or by initiating an alteration in bowel function. Late lesions will evidence similar complaints but also may cause pain by perineural involvement or disturbances in other proximate body systems such as the genitourinary tract. If the lesion tends to become obstructive, abdominal cramps, distention, anorexia, nausea, and vomiting are observed.

Growths that tend to grow into the bowel lumen instead of along the wall do not tend to obstruct until late and usually manifest themselves by bleeding and by causing a sense of incomplete evacuation after stool. Weight loss often parallels the seriousness of the tumor, but general symptoms such as malaise and lethargy may appear at any time.

The Physician

The doctor must sift and sort the subject's symptoms in order to evaluate the patient fully. Bleeding from the rectum

From the Department of Proctology, Temple University Medical School and Hospital, Philadelphia, Pennsylvania.

must be considered a sign of cancer until proved otherwise. The family doctor must examine each patient with this complaint thoroughly until the actual source of bleeding is discovered. The symptom of pain also deserves careful scrutiny. Sharp or intermittent pains at stool are probably anorectal in origin, but dull, vague pain, unassociated with the act of defecation, may suggest a more serious condition.

The examination of the patient should be thorough and systematic. His general appearance may suggest neoplastic disease by evidencing weight loss and anemia. Examination of the abdomen may show the telltale signs of obstruction with distention and increased bowel sounds. Evidence of metastases may be noted in hepatomegaly, ascites, or inguinal node enlargement. Jaundice, likewise, suggests a fateful spread of disease.

Examination of the rectum, of course, is a necessary step in any general, physical appraisal of a patient. The procedure is simplified if three steps are employed, namely: inspection, palpation, and visualization. If the examiner is right handed, place the patient on his left side with both thighs flexed. With good illumination inspect the anus and perianal integument for signs of any inflammatory or pathological entity that might explain the patient's symptoms. Next, insert the well-lubricated, gloved index finger into the anal canal in the direction of the umbilicus. This is the constant course of the anal canal and less discomfort will be caused by inserting the finger, as well as the speculum, in this direction. Palpate the anorectal line for crypts and papillae, then explore the normal rectal and perirectal landmarks. With gentle pressure in a rotating manner insert the finger as high as possible into the rectum taking care to palpate its wall throughout a 360-degree circumference. Frequently it is advisable to exert pressure on the lower abdomen with the other hand. Some examiners suggest utilizing the right lateral position with the left index finger in the rectum in order to free the sigmoid colon from the confines of the iliac fossa so that it may prolapse somewhat into the pelvis thus pre-

senting a longer segment of bowel to the probing finger.

The feel of a rectal cancer is difficult to forget. It is usually nontender, hard, and quite irregular. The polypoid or papillary tumors are friable and may be somewhat mobile, while the scirrhous growths are fixed and tend to ulcerate in the center. The edges of the tumor are rolled, raised, and everted.

Cancer of the rectum when visualized is reddish, lobulated, and surrounded by edematous, raised mucosa. Those practitioners familiar with taking biopsies should remove sections near the center of the tumor where less bleeding is likely to occur and where invasion is more prone to exist.

Diagnosis

The diagnosis of rectal cancer is suggested from the history of altered lower-bowel function and by the discovery of a firm, fixed, and frequently ulcerated mass which in most cases reveals irregular, rolled edges on visualization. Confirmation, of course, is obtained from the biopsy.

A barium enema with air-contrast studies plays an integral part in the complete evaluation of a patient with cancer of the rectum. Although it is difficult to study the rectum roentgenographically owing to its relative inaccessibility and immobility, the importance of ruling out obstruction and higher lesions cannot be overstressed. About 6 per cent of rectal and large bowel cancers will be multiple.¹

The differential diagnosis rarely presents a problem. However, there are a few confusing conditions worth noting. Normal landmarks can be puzzling to the infrequent examiner. The coccyx may be unduly prominent as palpated through the posterior rectal wall. The promontory of the sacrum, though always in the mid-line, may be irregular or unusually low. The cervix or a pessary in the female can become confusing as can the palpation of a bladder catheter, prolapsed ovary, or an enlarged fundus. Careful evaluation, however, should prove these masses to be ex-

traluminal. Impacted stool causes little concern, as it can be indented, whereas cancer cannot. Polyps of the rectum, of course, are closely allied with rectal cancer but will appear softer and more mobile to the touch. These, likewise, are more regular upon visualization and evidence less inflammatory reaction. Anal papillae are usually tiny but may enlarge to the size of a man's thumb. They always originate directly from the anorectal line and are covered with smooth, squamous epithelium. Internal hemorrhoids are palpable on occasion as soft swellings, while visualization reveals their identity as oval masses in two or three quadrants located immediately above the anorectal line. Abscesses are confused with tumors occasionally, but almost always they reveal the signs of inflammation with redness and tenderness. Not infrequently pus may be seen extruding from a connected, inflamed crypt and on occasion a communicating, fistulous tract may be palpated. Rectal strictures and those resulting from lymphopathia venereum are firm and fibrotic. Inguinal node swelling, a history of venereal disease, and a positive Frei skin test will usually establish this diagnosis. Foreign bodies are encountered mainly in mentally unbalanced patients and unless they become embedded in the wall of the rectum through long-standing chronic inflammatory cohesiveness, no diagnostic difficulties should be experienced.

Pathology

The pathology of rectal cancer in approximately 99 per cent of cases reveals adenocarcinoma, whereas the remaining 1 per cent consists of lymphosarcoma, leiomyosarcoma, and other rare tumors. This does not include squamous-cell carcinoma, which occurs in the anal canal and perianal integument.

Precancerous conditions are receiving more and more attention as the evolution of cancer is studied. It is the general consensus that polyps of the rectum are premalignant growths. The age and sex distribution is identical with that of the rectal cancer, the finding of rectal polyps in con-

junction with rectal cancer is suspiciously high, and the location of rectal polyps in the bowel is statistically the same as carcinoma. Then, too, actual, periodic observations of growing rectal polyps have been undertaken with eventual malignant change observed *in vivo*.³

Familial polyposis, which is a hereditary condition appearing usually by the third decade of life, is a well-known precancerous condition. Only 3 per cent of these patients will fail to develop cancer by the age of 50 years. Polyposis occurring during later years of life also must be considered a premalignant condition, although it probably is not on a familial basis.¹

Long-standing fistula-in-ano may be associated with cancer of the rectum. The growth may be small and insinuate itself along the ramifications of the fistulous tract where it becomes most difficult to remove.

Patients with chronic ulcerative colitis of more than ten years' duration develop cancer of the rectum and large bowel in a high percentage of cases. Fourteen per cent of our over-all operative specimens of ulcerative colitis show frank malignant change. This is especially true when pseudopolyposis of the bowel is present.⁴

Treatment

The treatment of rectal cancer lies as much in the eradication of the known precancerous lesions as in the removal of the malignant growth itself. All polyps or other suspicious growths must be removed and submitted to microscopy. If cancer is discovered, surgical removal must be undertaken. Youth is no barrier to radical surgery for polyposis.

Fistula-in-ano should be excised at an early date and the recurrence of sinus tracts held with some suspicion.

Ulcerative colitis should be attacked with therapeutic boldness. If medical management fails after a reasonable period of time, surgical extirpation of the diseased segments must be carried out. This is especially true if pseudopolyposis is present.

When the diagnosis of cancer of the

rectum has been made, the only treatment is radical surgical excision of the rectum and the lymph channels radiating from it. Local excision of even a small growth is not curative and should never be employed. Radiation is inefficacious in all but a few rare sarcomas. The operations of choice are many and varied, the selection being made on the location of the lesion and not on its size or anaplasticity.

Prognosis

The prognosis for cancer of the rectum is favorable. At present better than 54 per cent of our patients are alive and well over a period of five years or more following surgical removal of a rectal cancer. In the

absence of metastases we hope to cure at least 75 per cent for a similar period providing an extended and radical extirpation is undertaken and the diagnosis is made early. This is a challenge to the general practitioner and surgeon alike. Delay in diagnosis may be unavoidable in some cases, but all too frequently the patient or the doctor is inclined to shrug off mild intestinal complaints and to treat with indifference the occurrence of rectal symptoms.

Therefore, let the patients pay heed to nature's early admonitions and consult the family doctor. And, let the doctor take the patient's intestinal complaints to heart and carefully examine the rectum. One minute's time may save a life!

References

1. Bacon, H. E.; McElwain, J. W., and Trimpi, H. D.: Surgical management of large bowel lesions. *Bull. New York Acad. Med.* 29:34-46, 1953.
2. Department of Public Health, City of Philadelphia: *Health Bulletin*. [Annual Report, 1950.]
3. Jackman, R. J., and Mayo, C. W.: The adenoma-carcinoma sequence in cancer of the colon. *Surg., Gynec. & Obst.* 93:327-330, 1951.
4. Shands, W. C.; Dockerty, M. B., and Bagen, J. A.: Adenocarcinoma of the large intestine associated with chronic ulcerative colitis: clinical and pathologic features of 73 cases. *Surg., Gynec. & Obst.* 94:302-310, 1952.

Now-a-days, because of better preparatory measures and the judicious utilization of chemotherapeutic agents and antibiotics, patients come to the operating room in a state more nearly approaching physiological equilibrium than hitherto. A longer preparatory period permits adequate decompression and cleansing and sterilization of the bowel. The use of whole blood, high caloric diet, attention to protein and electrolyte balance and the co-operative assistance of internists and cardiologists, particularly in this period, have immeasurably forwarded surgery in this field. It is because of these factors, as well as the fact that a larger number of well-trained surgeons are operating upon these cases, that mortality figures have been reduced in expert and trained hands to well below 5 per cent—one might almost say to below 3 per cent as an average among mature surgeons.

Rankin, Fred W., and Graham, A. Stephens: *Cancer of the Colon and Rectum*. Springfield, Ill. Charles C Thomas, 1950.

The Second Look in Patients with Postoperative Symptoms of Carcinoma without Recurrence

Calvin Reed Brown, M.D.

Second-look operations of Wangenstein and his associates, following extirpation of abdominal cancer, have been used largely in asymptomatic patients. Little use has been made of these re-explorations in patients developing symptoms suggesting recurrence. The surgeon whose patient shows definite symptoms of recurrence of cancer often accepts defeat, pronounces the patient to be hopeless, and sends him home for terminal care. Many of these patients, despite the severity of symptoms and the apparently hopeless situation, can be remarkably relieved by second-, third-, and fourth-look operations.^{2,5} Such re-entry of the abdomen often demonstrates the absence of recurrence although the symptoms had closely simulated those of the cancer before extirpation. These symptoms may be due to cicatrization, benign-tissue reaction, post-irradiation or psychological reaction, or to coexisting disease.^{1,3}

The relief of anxiety of the patient and his family upon learning that there has been no recurrence fully justifies re-exploration in these patients. Three such cases were observed at the City of Hope Hospital for Cancer and Allied Diseases.

Case 1

A 45-year-old tailor developed vague pains in the back two years before admission in January, 1950. His appetite was poor. He complained of weakness. His right testicle was swollen. His physician found a tumor mass in the right abdomen that proved to be a 7½ lb. retroperitoneal liposarcoma, which was removed. Axillary and inguinal nodes showed lymphadenitis upon biopsy. Twenty months after opera-

tion the patient was readmitted for pain in the right flank and side of the abdomen from which he had never been free. He had anorexia and had lost 10 lb. in weight. The inguinal and axillary nodes were soft. There was tenderness and voluntary guarding of the upper and posterior abdomen. An intravenous pyelogram showed an inward curve of the right ureter. All these symptoms strongly suggested recurrence, and exploratory operation was performed twenty-one months after the initial removal. The entire abdomen and retroperitoneal space were grossly free from tumor. Upon learning that there was no recurrence, the patient rapidly improved psychically and symptomatically. He is now asymptomatic.

Case 2

A 69-year-old furniture dealer was admitted for rectal bleeding of a year's duration. The bleeding was slight until three weeks before admission when a sudden massive rectal hemorrhage occurred. His local physician reported a tumor of the rectum and referred the patient immediately for operation. Barium enemas revealed a polypoid filling defect high in the sigmoid colon. At operation a papillary adenocarcinoma, 6 cm. in diameter, was found involving the serosa near the mesenteric border at the sigmoid flexure. Regional lymph nodes were enlarged. Resection of the sigmoid and part of the descending colon and adjacent lymphatics was performed, with end-to-end anastomosis. There was no extension to other organs. Three days after discharge the patient was admitted with symptoms of in-

From the City of Hope Hospital, Duarte, California

testinal obstruction. Re-exploration revealed a pericolic abscess at the site of the anastomosis, with adhesions of the small intestine. This 3-in. segment of the small bowel was resected with end-to-end anastomosis and drainage of the abscess. Transverse colostomy was performed. Five months later barium enema revealed a constant stricture at the site of the anastomosis. Ten months after his first admission a second look was decided upon to rule out recurrence as the cause of the stricture. Only scarring and inflammation at the site of the stricture were found. Lysis of the adhesions was performed and the colostomy closed. The patient improved rapidly and is now asymptomatic.

Case 3

A 39-year-old tool and die worker developed dull sacral pain followed by constipation, rectal pain, and mucous discharge from the rectum. Sigmoidoscopy and biopsy revealed a carcinoma of the sigmoid. The sigmoid colon was resected with end-to-end anastomosis. Temporary transverse colostomy was performed and closed a month later. After a total absence from work of four months, he returned to his employment for a period of fifteen months and was asymptomatic. He then developed severe sacral and coccygeal

pain, radiating to the left buttock and down the back of the left thigh and leg toward the ankle, requiring narcotic therapy. The pain was not unlike that experienced before resection of the carcinoma and suggested recurrence to the patient and his physicians. Upon readmission sigmoidoscopy revealed an annular constriction of the sigmoid that appeared to be malignant, but biopsy showed it to be scar tissue. Exploratory laparotomy revealed all abdominal viscera to be normal except the gallbladder, which was literally bulging with small calculi. Cholecystectomy was performed. The leg pain remained and was probably some form of sciatic neuritis magnified by anxiety and fear of recurrence and entirely unrelated to the abdominal neoplasm or its removal.

Comment

These three cases illustrate the difficulty of determining recurrence without laparotomy, and the immense relief the second-look operation gives the anxious patient with symptoms simulating those of malignant extension, but really caused by benign complications or by unrelated intercurrent disease. The large-bowel-cancer postoperative patient, even when apparently hopeless, should not be denied the benefit of second-look surgery.

References

1. Berne, C. J., and Freedman, M. A.: Local recurrence following subtotal gastrectomy for carcinoma. *Am. J. Surg.* 82: 5-7, 1951.
2. Lewis, F. J., and Wangenstein, O. H.: Explorations following resection of the colon, rectum, or stomach for carcinoma with lymph node metastases. In *Surgical Forum: Proceedings of the Forum Sessions, Thirty-Sixth Clinical Congress of the American College of Surgeons*; Boston, Massachusetts: October, 1950. Philadelphia, W. B. Saunders Co., 1951.
3. Peltier, L. F.: The search for lymph node metastases in cancer of the rectum. *Surgery* 30: 443-447, 1951.
4. Wangenstein, O. H.: Cancer of colon and rectum: with special reference to (1) earlier recognition of alimentary tract malignancy; (2) secondary delayed re-entry of the abdomen in patients exhibiting lymph node involvement; (3) subtotal primary excision of the colon; (4) operation in obstruction. *Wisconsin M. J.* 48: 591-597, 1949.
5. Wangenstein, O. H.: The cancer problem today. *Journal-Lancet* 69: 344-350, 1949.
6. Wangenstein, O. H.: The surgeon's approach to the problem of alimentary tract malignancy. *Journal-Lancet* 70: 411-419; 450, 1950.

Exfoliative Cytology in Disorders of the Colon

A Preliminary Report

*Clarence C. Fuller, M.D., Harold E. Clark, M.D., E. L. Hecht, M.D.,
and Clifford Cohen, M.D.*

Exfoliated cells from the lining of the gastrointestinal tract have been used for diagnostic purposes since 1903 by Fletcher and later, in 1907, by Jürgens. In 1909 Marini diagnosed thirty-two out of thirty-seven gastric carcinomas on unstained cells in washings from the stomach. Bahr² in 1910 and Bartlett in 1917 used cytological studies in dysentery. In the same year Wenyon and O'Connor separately suggested that study of cellular exudates might be of value in conditions other than amebic and bacillary dysentery. In 1940 Bercovitz demonstrated that, if pathological changes occur in the bowel mucosa, cells of various types are present in the discharges; he reported one case of carcinoma of the rectum, one of carcinoma of the splenic flexure, and one of polyps in the terminal ileum. All of these showed a heavy cellular exudate, which he felt was one of the earliest evidences of pathological changes in the lower bowel. In 1941 interest in this method of diagnosis was stimulated by the work of Papanicolaou and Traut, and since that time much has been written on exfoliative cytology in the diagnosis of lesions in all parts of the digestive tract. In 1951 Bader reported on 200 cases in which smears were made from the rectal washings if the lesion was within reach of the sigmoidoscope, and from colonic washings when the lesion was beyond. She reported on nineteen cases proved malignant by biopsy and surgery, of which eighteen had positive or suspicious smears; one reported as a benign polyp was later proved malignant; there were no false positives.

Bader stated that the cytology in smears from the bowel consists of columnar and squamous cells from the anus, cuboidal cells from the crypts of Lieberkühn, and goblet cells in 50 per cent of

the cases of polyps; the malignant cells are identified by their characteristic features.

In 1949 Wisseman, Lemon, and Lawrence reported on twenty-eight cases of proved carcinoma in which smears from the lesion or from the discharge were taken. Nine were positive (four in the rectum and rectosigmoid and five in the sigmoid); seven, questionable (three in the rectum and rectosigmoid, four in the sigmoid); and twelve, false positives (two in the rectum and rectosigmoid and three in the sigmoid, and seven in the ascending and transverse colon were missed).

In 1953 Hecht and Cohen reported the three types of cells usually found in smears from the colon and stated that the criteria for diagnosing carcinoma in these smears are the same as for carcinoma elsewhere, namely, cells with (1) a fairly distinct cellular border, (2) vacuolated cytoplasm, (3) greatly enlarged eccentric nuclei, (4) increased amount of and heavily clumped nucleochromatin, and (5) heavily stained nuclei. In five of their positive cases there was no visualization of the lesion by sigmoidoscopy.

A detailed study of cytological diagnosis in the gastrointestinal tract was recently reported by Rubin, Massey, Kirsner, Palmer and Stonecypher in 300 cases over a two-year period. They stated that in the colon, cytological study is unnecessary in lesions accessible to the sigmoidoscope but is valuable in diagnosing lesions of the distal colon. They made a positive cytological diagnosis in three carcinomas of the cecum and one of the hepatic flexure. Difficulties were encountered with

From the departments of Medicine and Surgery, New York University Post-Graduate Medical School, and the Gynecology-Cytology Laboratory, University Hospital, New York, New York.

This study was facilitated by the Frances Scott Memorial Fund Grant.

Grateful acknowledgment is made to Mr. Raymond Cook, A.B. for technical assistance and to Mrs. Lettie Winston for clerical assistance.

polyps diagnosed as malignant adenomas, referring to noninvasive histologically malignant polyps. They reported twenty-two benign lesions all correctly diagnosed on the initial cytological examination; twenty-seven of thirty-three proved malignant lesions of the colon were diagnosed preoperatively by cytology. They found the cytological method useful in differentiating benign from malignant polyps and said it might be an aid in cases with persistent occult blood in the stools, when all other studies are negative.

Case Selection

The present study was undertaken to determine if cytological examinations are of value in the diagnosis of various disorders of the colon, especially in the early diagnosis of malignancy. No special types of cases were chosen. Mackenzie and Hecht, in 1948, diagnosed the first case of carcinoma of the rectosigmoid by rectal smear, at the University Hospital, using the Papanicolaou staining technique. From 1947 to 1951 fifty-one cases were examined. These included eight carcinomas, of which four had positive smears, two were suspicious, and two were reported negative. Four cases of nonspecific diarrhea, two of rectal stricture, fifteen of ulcerative colitis, one polyp, two benign growths, one case of diverticulitis, four of rectal bleeding and proctitis, and ten without clinical diagnosis, all showed negative smears; two specimens were unsuitable for staining. Smears were made in a variety of ways, including specimens on plain gauze, slides in acetone, fluid washings, etc.

In 1952 the present study was started. The majority of smears were made directly from the lesions through the sigmoidoscope. Others were taken from the lesions using an abrasive balloon, and in a few cases from the bowel wall above the sigmoidoscope when the lesions were not visible through the instrument. Technical difficulties have prevented the accumulation of sufficient balloon smears for comparison with direct smears, but this work is continuing.

Preparation of Patients

Patients were prepared for examination by two enemas of normal saline, 8 oz. each, the first to be given one hour and the second one-half hour before examination. To avoid irritation of the bowel no laxatives are used.

A standard sigmoidoscope is used for all examinations. Patients are placed in the knee-chest position, and aspiration of retained fluid or washing of the mucosa is accomplished with a sigmoid cannula, using warm saline. Smears are made with a sponge-rubber swab; cotton swabs are avoided, as strands of cotton adhere to the slide. The smears are immediately placed in a fixative solution of equal parts of 95 per cent alcohol and ethyl ether.

The entire procedure is simplified so that it can be carried out as a routine office or clinic procedure and no special apparatus is necessary.

Number of Patients and Results

A total of eighty-three patients have each received from one to six examinations. All patients with carcinoma, ulcerative colitis, or polyposis have been re-examined at intervals of three months when possible.

In our series there were five carcinomas; four within reach of the sigmoidoscope have had positive smears (Figs. 1, 2) and have been confirmed pathologically. The one false negative was a carcinoma of the hepatic flexure (Fig. 3) later confirmed pathologically. Of four previously resected carcinomas two were in the sigmoid colon, one at the hepatic flexure, and one in the ascending colon. Of these, three cases continue to give repeated negative smears two to five years after surgery. One in the sigmoid colon, which had been resected four years previously, has recently been found to be cytologically suspicious and is being thoroughly investigated.

There were two cases of malignant polyps removed surgically four to six years ago. One of these continues to give negative smears; the other recently became

positive with the appearance of another polyp at or near the site of the one previously removed. There were eight cases of benign polyps, which repeatedly gave negative smears; two of these had rectal polyps removed three to eight years previously.

Four cases of active ulcerative colitis, with evidence of polyps, had repeatedly negative smears. In six additional cases of active ulcerative colitis, with polyps, two were read as positive; these cases have since undergone total colectomy because of malignant change. In the other four cases, two were read as positive, two as suspicious. In nine other cases of active ulcerative colitis, with no evidence of polyps, all smears were negative.

In two cases of infective ulcerative colitis, smears taken from small sessile rectal polyps 2 to 3 mm. in diameter (Fig. 4) were positive (Figs. 5, 6). The polyps were fulgurated and smears from the areas have been consistently negative since. Seventeen other cases of inactive ulcerative colitis have all been consistently negative.

Other cases examined include three of

diverticulitis, four with normal mucosa, three with hemorrhoids, five with constipation, one with ileocecal tuberculosis, three with proctitis, two with scleroderma, two with intestinal parasites, and three with regional enteritis. Smears in all of these were negative. One other case of regional enteritis, ulcerative colitis, and pyoderma had a positive smear and has had a colostomy.

Summary

1. The role of exfoliative cytology using the Papanicolaou staining technique in diagnosing cancer of the large bowel is reviewed.

2. A brief summary of 134 cases studied at this hospital is presented.

3. Particular attention is directed toward the use of this method in the early diagnosis of malignant polyps and in the follow-up of extirpated malignant lesions of the colon.

4. Further investigation of a method for obtaining specimens beyond the reach of the sigmoidoscope (abrasive balloon) is being carried on.

References

1. Bader, G.: The cytologic picture in rectal and colon pathology. In *Proceedings; Symposium on Exfoliative Cytology*, October 23-24, 1951. New York: American Cancer Society, Inc. [1953]; pp. 82-86; disc. 86-88.
2. Bahr, P. H.: Report to the London School of Tropical Medicine on investigations on dysentery in Fiji during the year 1910. *J. London School Trop. Med. Suppl.* 2: 1-77, 1912.
3. Bahr, P. H.: A study of epidemic dysentery in the Fiji Islands, with special reference to its epidemiology and treatment. *Brit. M. J.* 1: 294-296, 1914.
4. Bartlett, G. B.: Pathology of dysentery in the Mediterranean Expeditionary Force, 1915. *Quart. J. Med.* 10: 185-244, Pl. 26-34, 1917.
5. Bercovitz, Z.: Studies in cellular exudates of bowel discharges. I. Control observations in 1,123 patients, 7 autopsies, and 3 dog experiments. *J. Lab. & Clin. Med.* 25: 788-795, 1940.
6. Futcher, T. B.: A study of the cases of amoebic dysentery occurring at the Johns Hopkins Hospital. *J. A. M. A.* 41: 480-488, 1903. Cited by Bahr.²
7. Hecht, E. L., and Cohen, C.: The cytologic method in gastrointestinal cancer. *Rev. Gastroenterol.* 20: 11-20, 1953.
8. Jürgens: Die Amöben-Enteritis und ihre Beziehungen zur Dysenterie. *Zschr. f. exper. Path. u. Therap.* 4: 769-816, Pl. XXIV-XXVII, 1907. Cited by Bahr.²
9. Mackenzie, L. L., and Hecht, E. L.: A case of carcinoma of the rectum diagnosed by the cytologic method. *Rev. Gastroenterol.* 15: 915-916, 1948.
10. Marini, G.: Über die Diagnose des Magenkarzinoms auf Grund der cytologischen Untersuchung des Spülwassers. Eigene Beobachtungen über den normalen und pathologischen Zelleninhalt des Magens. *Arch. f. Verdauungskr.* 15: 251-267, 1909.
11. Papanicolaou, G. N., and Traut, H. F.: The diagnostic value of vaginal smears in carcinoma of the uterus. *Am. J. Obst. & Gynec.* 42: 193-205; disc. 205-206, 1941.
12. Rubin, C. E.; Massey, B. W.; Kirsner, J. B.; Palmer, W. L., and Stonecypher, D. D.: The clinical value of gastrointestinal cytologic diagnosis. *Gastroenterology* 25: 119-138, 1953.
13. Wenyon, C. M., and O'Connor, F. W.: *Human Intestinal Protozoa in the Near East: an Inquiry into Some Problems Affecting the Spread and Incidence of Intestinal Protozoal Infections of British Troops and Natives in the Near East, with Special Reference to the Carrier Question, Diagnosis and Treatment of Amoebic Dysentery, and an Account of Three New Human Intestinal Protozoa*. London: John Bale, Sons & Danielsson, Ltd. 1917.
14. Wiseman, C. L., Jr.; Lemon, H. M., and Lawrence, K. B.: Cytologic diagnosis of cancer of the descending colon and rectum. *Surg., Gynec. & Obst.* 89: 29-30, 1949.

(Figures 1 to 6 appear on opposite page.)

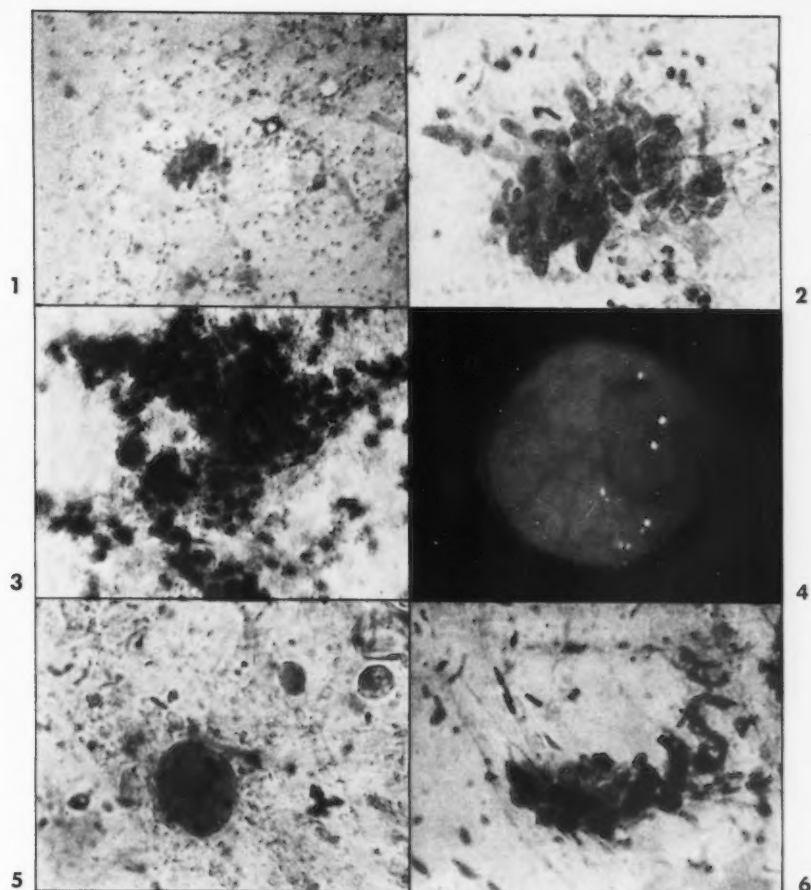


FIGURE 1. Direct smear from the carcinoma of the rectum, low power, showing a group of malignant cells in the center of the field.

FIGURE 2. Direct smear from carcinoma of the rectum, high dry power, of the suspicious cells in Figure 1, showing the characteristics of malignant cells.

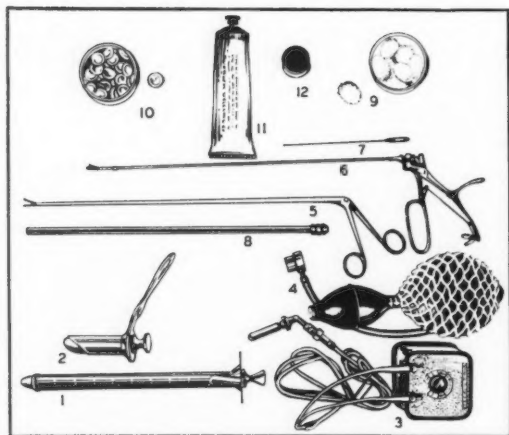
FIGURE 3. Smear in inflammation of the colon, showing polymorphonuclears and erythrocytes but no malignant cells.

FIGURE 4. Rectal polyp, seen through the sigmoidoscope.

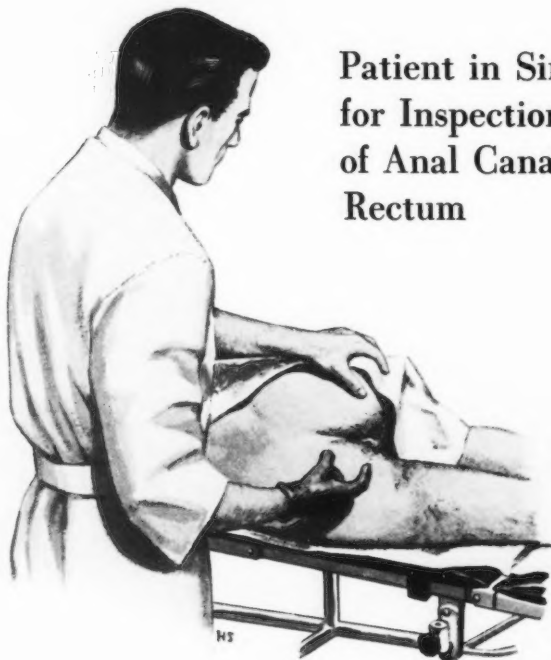
FIGURE 5. Direct smear from the bowel wall around the polyp in Figure 4, showing scanty cellular exudate and no malignant cells.

FIGURE 6. Direct smear from the polyp in Figure 4, showing malignant cells with characteristic features.

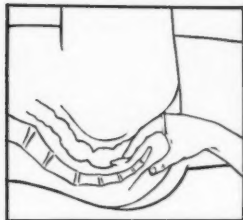
Palpation and Visualization



Minimum Equipment Necessary for Rectal Examination. (1) 25-cm. sigmoidoscope; (2) anoscope; (3) battery, cords, and sigmoidoscope light; (4) window and inflation bulb; (5) alligator forceps; (6) biopsy forceps; (7) flexible probe; (8) suction rod; (9) cotton sponges; (10) finger cots; (11) tube of lubricant; (12) small container for biopsy specimens



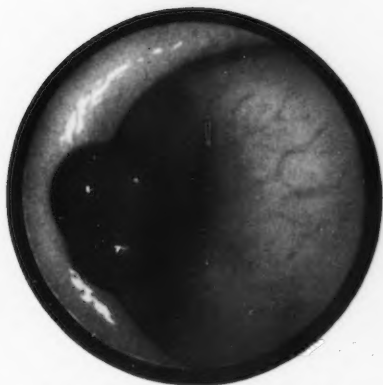
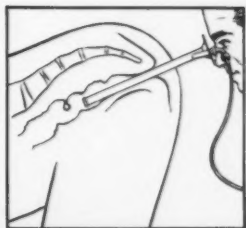
Patient in Sims Position for Inspection and Palpation of Anal Canal and Lower Rectum



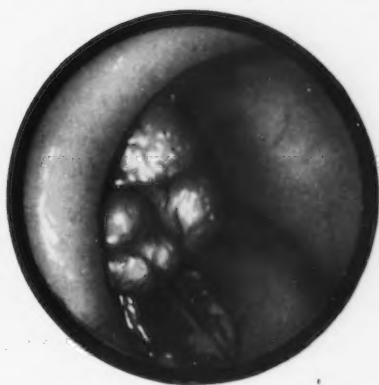
Simple Office Procedures



Patient in Knee-Shoulder Position for Sigmoidoscopic Examination



An adenoma as viewed through a sigmoidoscope



A cancer in an anemic patient as viewed through a sigmoidoscope

Adenomatous Polyps of the Colon and Rectum

Robert Turell, M.D.

Not all colorectal adenomas become cancers, but 10 to 20 per cent of cancers of the large bowel originate in adenomas. Since there are no gross or microscopic criteria that will enable the proctologist or the pathologist to predict a benign course for a given adenoma, it is best to extirpate this lesion immediately upon recognition as a matter of cancer prophylaxis. Since many colonic polyps are situated within the reach of a 25-cm. sigmoidoscope, every comprehensive physical examination should include sigmoidoscopy.³ This examination does not require a proctologist; many progressive internists, general practitioners, and general surgeons have trained themselves to perform sigmoidoscopy. They refer patients to the proctologist for definitive treatment of adenomas following their sigmoidoscopic examinations.

Classification

Current knowledge does not justify a complex classification nor is it desirable, as it tends toward confusion. Recently an attempt has been made to discard the grossly descriptive term "villous" and to substitute for it the microscopically descriptive term "papillary." Unfortunately papillary adenomas are readily confused with anal papillae, which are benign fibroepithelial polyps. Nor does the term "papillomatous" appear to be an improvement. Gross descriptive terms (Fig. 1) have simple teaching value. A classification of adenomas into (1) smooth or villous, (2) pedunculate or sessile, and (3) benign or malignant is simple and logical. Malignancy in adenomas is best described as noninvasive or preinvasive or invasive—these terms have vivid meanings to all clinicians.

Pathology

Reports of adenomas of the large bowel should state the definitions and criteria of histological examination so that the basis for diagnosis may be clear. The proctologist and the pathologist must work in close liaison and use the same terminology. It is not oversimplification to consider an adenoma as a pedunculate or sessile glandular structure showing proliferation of intestinal epithelium without invasion of the muscularis mucosae or lymph channels or blood vessels. Histologically, adenomas consist of hyperplastic, relatively mature or well-differentiated epithelial cells of uniform appearance supported by a central core of loose connective tissue. They contain stalks of varying numbers, sizes, shapes, and lengths, which differ from the normal colonic mucosa in which a single layer of cells lines the crypts and covers the surface. Some of the cells contain a rich complement of mucus and closely resemble normal colonic epithelium. Other cells contain little or no mucus, are stratified, and exhibit a fair number of mitoses. Unless secondary infection or ulceration has taken place, no significant inflammation is found in adenomas or their supporting tissues. However, when pronounced dedifferentiation is present, the lesion is considered an early, preinvasive or noninvasive malignant transformation, which may occur as a small focus (called carcinoma *in situ* by some authors). This reversion to the more immature or undifferentiated type of cell may be indicated by atypism, large vesicular or hyperchromatic nuclei, frequent mitoses, and excessive stratification. When there is invasion of mucosal connective tissue through the basement membrane or the muscularis mucosae or of

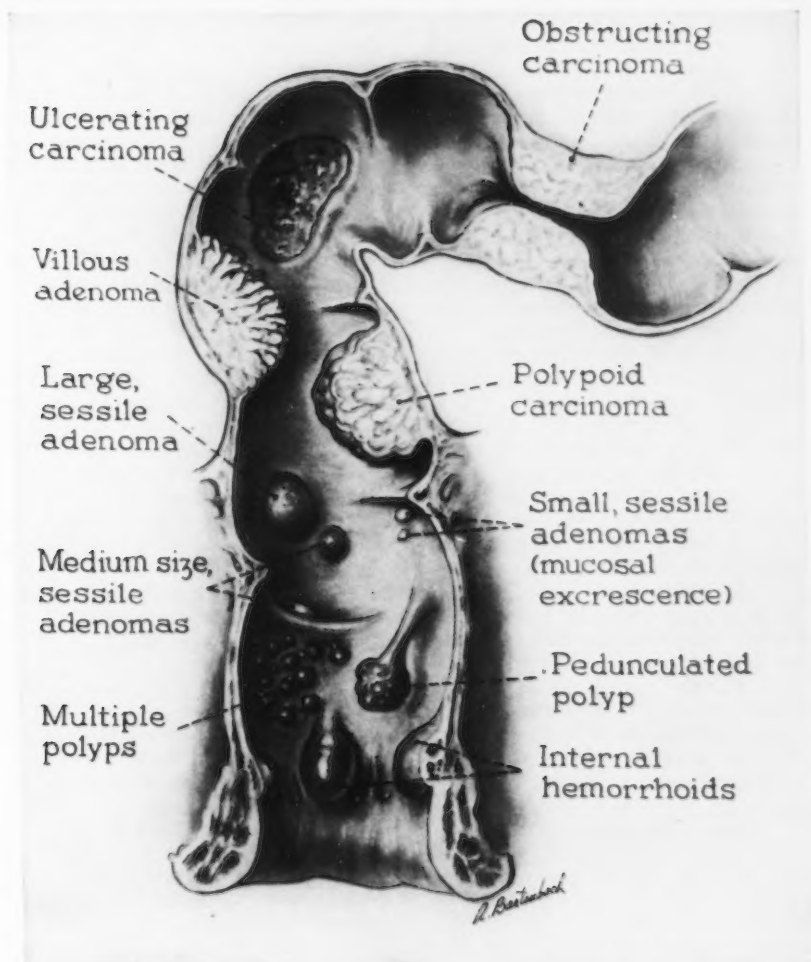


FIGURE 1. Lesions of the large bowel.

the blood vessels or the lymph tracts, the lesion is regarded as a frank carcinoma.¹ The term "invasive adenoma" should be abandoned and superseded by the term "cancer" in order to avoid the misleading benign connotation.²

Villous adenomas originate in the cells of the surface epithelium, and the lobulated polyp arises from the cells lining the

intestinal mucous glands. Clinically the villous adenoma occupies a position midway between benign nonvillous adenomas and adenocarcinoma. Grossly, the villous growths are sessile, soft, spongy, solitary and large, occasionally filling the entire lumen of the bowel. They are usually found in the rectum or rectosigmoid and seldom in the colon. Villous growths occur

most often in the sixth and seventh decades of life and are rare in comparison with other types of adenoma or adenocarcinoma. Recurrence following any type of therapy and a pronounced propensity to undergo malignant transformation are outstanding features of this lesion.

Microscopically, the villous adenoma may be benign, malignant, or atypical. The malignant portion may exist as isolated foci of noninvasive adenocarcinoma within a small remnant of the original benign villous tissue. The cancerous transformation is believed by some to occur in any part of the growth and by others, deep in the base, frequently without surface evidence of its presence.

Personal sigmoidoscopic and roentgenological studies of large groups of patients, more than 50 years of age, with proctological symptoms—primarily rectal bleeding—show an incidence of 7 per cent of microscopically verified adenomas, exclusive of mucosal excrescences. In asymptomatic individuals the incidence is 2 per cent, 4 per cent if mucosal excrescences are considered. Mucosal excrescences may show carcinomatous transformations. Attempts to follow by periodic endoscopic examinations and biopsies the possible transition of adenomas to carcinomas failed from lack of patient co-operation.

Diagnosis

The diagnosis of adenomas situated within the reach of the sigmoidoscope is best made by endoscopy and "total biopsy." The polyp is removed at or with the base in toto or in several large segments for microscopy in order to detect promptly any small malignant foci within the adenoma or at its base.

For the detection of polypoid growths situated above the reach of the sigmoidoscope, main dependence is placed on pre-operative radiography and on digital or manual transabdominal exploration during the course of operation. In the hands of capable roentgenologists or gastroenterologists, special roentgenological techniques such as the tannic acid method with barium sulfate and air have real

merit, while the standard barium enemas leave very much to be desired, particularly as far as the detection of small adenomas is concerned. The differentiation of fictitious from true polyps is sometimes most difficult. Surgery should not be used for polyps situated beyond the reach of the sigmoidoscope unless two consecutive roentgen-ray studies of the colon reveal the lesion in the same relative position. Close co-operation between the roentgenologist and the proctologic surgeon should be maintained and is as essential as the latter's co-operation with the pathologist.

At operation, the entire colon from the cecum to the anus is gently and carefully palpated between the thumbs and the index fingers of both hands and sometimes transilluminated. Obese patients with large epiploic appendages offer considerable diagnostic difficulty. Occasionally, direct inspection by instrument of the interior of the colon through a colotomy incision is necessary. However, the precise value of endoscopy through small colotomy incisions remains to be assessed.

Treatment

For therapeutic considerations adenomas are divided broadly into those situated within and those above the reach of the sigmoidoscope.

Benign Neoplasms. MUCOSAL EXCRESCENCES. Mucosal excrescences and tiny sessile or pedunculate adenomas are extirpated in toto at the base with the cold, angulated biopsy forceps, and the base is desiccated with a ball-tipped electrode and submitted for histopathological examination. At times, after preliminary biopsy, the remainder of the lesion is destroyed electrothermically either by means of a ball-tipped electrode or a curved alligator forceps. Diathermic destruction of any mucosal elevation of the large bowel without preliminary biopsy is unwise.² Recto-sigmoid mucosal elevations only 2 to 3 mm. in diameter have proved to be adenocarcinomas, carcinoids, and leiomyoma.

PEDUNCULATE ADENOMAS. These lesions are removed at the base by means

of a high-frequency snare. Adenomas that are situated below the peritoneal reflection are usually treated in the office, while those located above the peritoneal reflection, the mobile portion of the terminal bowel, are treated in the hospital. When looping of the pedicle is technically difficult or unsafe, the adenoma may be removed by means of a clamp and specially designed scissors.

SESSILE ADENOMAS. Small- or medium-sized sessile adenomas located on the posterior and lateral walls of the rectum may also be successfully extirpated by means of the electric snare. Large sessile adenomas that are located below the peritoneal reflection are removed by means of the electric double-loop resector.² Adenomas situated in the more inaccessible areas, such as the upper surface of a rectal valve, are extirpated with relative ease, although in these situations both the adenoma and the rectal valve have to be excised in some cases. Most of the tissue thus resected retains sufficient of the original architecture for adequate histopathological examination.

For very large villous adenomas, radical resection similar to that for frank cancer is advisable.

Fractional or serial coagulation of sessile adenomas is unwise.

The detailed technique of the use of either the high-frequency snare or the double-loop resector has been described elsewhere.² It may be stated here that the safe use of either instrument requires considerable experience and some dexterity.

Malignant Neoplasms. NONINVASIVE. Adenomas with narrow or broad pedicles may be extirpated by means of the electrothermic snare with uneventful healing of the bases and without recurrence for from one to five years. Preinvasive malignant foci are seldom encountered in sessile adenomas; these are either invasive cancers at the start or totally benign. When such malignant lesions are found in sessile adenomas, they are best treated by intestinal surgical resection rather than by electrothermia or local excision.

INVASIVE. "Invasive adenomas" are regarded as frank cancers and are accorded

radical therapy consistent with the modern concepts of good cancer surgery.

ADENOMAS SITUATED ABOVE REACH OF THE SIGMOIDOSCOPE. Pedunculate adenomas. Polypectomy through a transabdominal colotomy is a safe and adequate operation for benign pedunculate adenomas: (1) if its body and stalk are firm or impressionable but not if hard or indurated, (2) if its pedicle or stalk is narrow, long, soft, and freely movable at its base, and (3) if the subjacent mesentery is free from palpable lymph nodes. In the presence of induration of any part of the polyp or fixation at the base with or without palpable mesenteric lymph nodes, segmental colonic resection with the mesentery should be performed. Examination of frozen sections of the specimen immediately upon excision is believed by many experienced pathologists to be unreliable unless most of the specimen is diffusely invaded by cancer; isolated malignant foci can seldom be detected with certainty by this diagnostic procedure.

Adenomas appearing to be benign on gross and/or on frozen-section examinations can be adequately removed by local excision. The diagnosis of malignancy is made only on evidence of actual invasion by malignant cells through the basement membrane or muscularis mucosae and not simply on the penetration of the base of the adenoma.

In recent years the routine resection of the polyp-bearing segment of bowel has been advocated for the extirpation of all pedunculate adenomas situated above the reach of the sigmoidoscope. This procedure is advised because in a few cases regional lymph-node metastases have been encountered in the absence of invasion of the pedicle. About seven sigmoid colons are unnecessarily resected to accomplish the proper operation for one cancer. However, this operation appears justified because, in the hands of some surgeons, polypectomy through colotomy and segmental resection are comparable in magnitude and subject to practically the same complications.

This radical operation is, by some, deemed unnecessary for noninvasive car-

cinomatous pedunculate adenomas. This surgical experiment should nevertheless be encouraged providing the morbidity and mortality are not increased following the more radical operation.

Sessile adenomas. These adenomas should be treated by segmental resection of the colon with a wide V-shaped area of the mesentery so as not to miss the opportunity for cure of a grossly undetected cancer. It is particularly important to treat villous adenomas of the colon by segmental resection.

Preoperative Treatment. The principles of preoperative preparation with respect to the oral employment of nonabsorbable or sparsely absorbable antibiotic and sulfonamide chemotherapy compounds are now almost universally accepted. In addition, broad-spectrum antibiotics, such as terramycin, are employed for their systemic effects.

Follow-Up Observation

Periodic endoscopic and roentgenoscopic examinations should be made for the lifetime of all patients in whom adenomas have been removed, in order to detect new or recurrent lesions at the earliest time.

Pediatric Aspects

Juvenile adenomas present a microscopic architecture similar to that of ade-

nomas in the adult except for a greater amount of connective-tissue stroma. The connective-tissue cells in these polyps are larger and more plump and there is generally a greater amount of inflammatory-cell infiltration. Malignant transformation may take place in polyps of infants and children.

The treatment of juvenile adenomas is essentially the same as that for adenomas in adults.

Geriatric Aspects

Adenomas of the terminal colon that are within reach of the sigmoidoscope should always be removed promptly upon recognition. Special caution should be used in application of electrothermia, particularly in the employment of the high-frequency snare because of the presence of sclerotic vessels in the pedicle. Low-intensity coagulating spark-gap current is applied and the pedicle is strangulated very gradually before it is finally severed. Tube current alone is best avoided. Symptomatic adenomas that are situated above the reach of the sigmoidoscope should also be removed promptly. However, senescent patients with asymptomatic adenomas located above the reach of the endoscope that are found incidentally on roentgen-ray examination should be individualized. Surgical therapy is sometimes withheld in very aged patients who can be followed by means of periodic roentgenoscopy.

References

1. Turell, R.: *Treatment in Proctology*. Baltimore. The Williams & Wilkins Co. 1949.
2. Turell, R.: *Tumors of the rectum*. [Correspondence.] *J. A. M. A.* 142: 277, 1950.
3. Turell, R., and Garson, B. J.: *Sigmoidoscopy and biopsy*. *New York State J. Med.* 50: 89-92, 1950.

The Management of My Colostomy

A Colostomy Patient

Eleven years ago, when I was 23 years old, after many unhappy years of painful and unsuccessful attempts to cope with ulcerative colitis and its effects, I had a temporary colostomy performed and, seven years later, a permanent colostomy. No malignant process was discovered, although my doctor assured me that, unless the permanent colostomy was performed at that time, there would have been a very high probability of such a condition subsequently.

Following my first operation I developed a routine of taking care of my colostomy that allowed me the most freedom of action and, at the time same, was the least restrictive.

I have been able to achieve excellent control of my colostomy by a combination of daily enemas, regular eating habits, and the use of a specially designed plug that prevents sudden small discharges of gas.

For my enema, which I take daily before breakfast immediately after arising, I use 1½ qt. of slightly more than lukewarm tap water, in an ordinary enema bag, with a no. F-22 catheter, connected by a glass tube, which indicates the rapidity of flow of water, with a simple metal shut-off device attached. I find that by using a plastic sleeve-type commercial irrigator, which is attached to a metal ring held against the body with an elastic belt and secured by a metal clip, I can move around my apartment while my colostomy is emptying, and I usually utilize this time in making my bed, preparing breakfast, and shaving. I have also found from experience that my best results are achieved by placing the enema bag on a hook on the bathroom door, about 72 in. from the floor; I then sit on the floor while taking the water. Usually most of the first 1½ qt. of water will not enter the colostomy opening on the first try. Therefore, I empty the unused COOLED water from

the sleeve-irrigator into a measuring cup, thus ascertaining how much replacement water I need. After discarding that water I put a like amount of fresh, WARM water into the enema bag. Almost invariably this second attempt is successful, and my bowels usually empty within thirty minutes from that time.

I always take a shower afterwards, at which time I scrub the plastic sleeve with soap and water and hang it to dry on a peg just inside my shower stall, which thus eliminates practically all odor.

There are very few foods that I avoid and, for the most part, they are the same foods that caused me trouble before my first colostomy operation. Of course, foods that should be avoided vary from person to person, but there are also some items that could cause trouble to all persons with colostomies, including carbonated beverages and leafy vegetables such as cauliflower and cabbage.

Rather than stressing the importance of eating and avoiding any specific food or foods, I have found that I have been able to get and keep very good bowel control by eating at regular times and about the same quantities each day. I also found that most medicines, especially aspirin, interfere with my colostomy irrigation. When I must take medicine I try to plan my activities more carefully that day, avoiding social commitments at night.

Also, I find that I must have a minimum of seven hours' sleep per night, preferably eight hours, in order to feel my best. Now and then I have considerably less than that for one or two nights with no bad results, but regular, sufficient sleep at night is a "must."

Although I work in a fairly large office, to my knowledge no one is aware that I have a colostomy. I've found that with the possible exception of horseback riding there is no sport in which I cannot participate. I especially enjoy swimming

and have encountered no embarrassing situations because of my colostomy, although I have to be careful in dressing and undressing.

I have found that when I am physically very tired or mentally upset I am prone to somewhat excessive gas discharges, and accordingly I try to avoid social engagements at such times. However, if I cannot avoid them, I find that a pneumatic plug, which was designed by

a Seattle surgeon, is very effective in preventing such discharges. Once I became used to this plug, I found it quite comfortable and it has been a tremendous help.

I have felt so much better and have enjoyed life so much more during the eleven years since my colostomy operations that the few restrictions and inconveniences mentioned here are much more than compensated for.

Carcinoma of the Rectum and Colon at the Lahey Clinic

RICHARD B. CATTELL, M.D. AND BENTLEY P. COLCOCK, M.D.

At the request of the American Cancer Society, Inc., we have summarized previously reported and unreported studies from this clinic of malignant tumors with particular reference to operability, mortality, and end results. In a series of 572 patients who were operated on between 1941 and 1945, of 335, who had neither lymph node nor blood vessel involvement with carcinoma in the resected specimen, 200 (59.7 per cent) survived five years. Of 55 patients who had both lymph-node involvement and blood vessel invasion, only 6 (10.9 per cent) survived five years. In a review of 103 patients with carcinoma of the cecum and ascending colon who were followed for five to ten years or more 50.5 per cent survived for over five years. Of those patients with metastases to the mesenteric lymph nodes in the resected specimen only 11 out of 41 (26.8 per cent) survived for five years.

In 1940 all patients were subjected to a two-stage modified type of Mikulicz resection, in 1945 80 per cent were operated on by this type of procedure, and in 1949 only 1.4 per cent had a two-stage resection while 98.6 per cent were operated on by the one-stage resection with primary anastomosis. The corresponding mortality rates for these periods were 10.5 per cent for 1940, 2.4 per cent for 1945, and 2.8 per cent for 1949. The corresponding operability rates were 82.8 per cent for 1940, 86.5 per cent for 1945, and 88.4 per cent for 1949. A similar reduction in the mortality rate along with the maintenance of a high operability rate was found for patients with carcinoma of the rectum and rectosigmoid. The mortality for 1940 was 16.5 per cent; for 1945, 7.8 per cent; and for 1949, 2.3 per cent. The corresponding operability rates were 89.2, 81.4, and 96.4 per cent. The operability rate of 96.4 per cent for all patients with carcinoma of the rectum at the present time is an indication of our belief that resection of the growth is a worth-while procedure in every patient with carcinoma of the rectum in whom it is technically possible to remove it. An operability rate of 90 per cent and a mortality rate of less than 3 per cent indicate that any further significant improvement in the end results of the treatment of cancer of the colon and rectum must come from earlier diagnosis and the detection and elimination of the premalignant mucosal polyp.

The benign mucosal polyp of the colon or rectum is a definite premalignant lesion which unfortunately is asymptomatic in more than 50 per cent of cases. Only by the increased use of the proctoscopic examination as a part of the complete physical examination will more of these premalignant lesions in the rectum and rectosigmoid be discovered. It is our belief that the increased use of proctoscopic examination not only will permit the detection of these premalignant lesions but also will make possible the detection of existing carcinoma of the rectum and rectosigmoid at a stage when resection will effect a cure.

Cancer of the Stomach Need Not Be Feared*

Toyozo Nitta

The preface by Dr. Ychiro Okada, Director, Prefectural Hospital, Shinjo City states:

It is my profound joy that Mr. Nitta is going to publish his own handwriting to inform the numerous cancer sufferers of his precious experiences. Without any hesitation, therefore, I can recommend everybody to read these valuable lines that will surely be both enlightening and encouraging.

Under the heading, An Early Diagnosis—The Only Way to Cure Gastrocirrhosis, the author writes:

First of all, I must tell my readers that I am a businessman, not a doctor. So, every reference to medical knowledge in this handwriting is entirely based upon what I have heard from my doctors, without adding anything from my own opinion. Of course, I shall be responsible for mishearings, if there be any.

The author then describes his diagnosis and his encounter with surgery, leading into his postoperative experiences with the heading:

The Long-Waited-For Ejection of Fart

Now, there must be a fart coming out within forty-eight hours after the operation, and until this time I was ordered to keep myself in absolute rest, without making a slightest motion or even taking a drop of water.

At last, on the third day the long-awaited-for fart came out. It was really a phenomenon eagerly expected by all concerned.

Doctors always feel finally relieved of anxiety because this proves the connection between stomach and intestines and also the beginning of vermiculation. It showed that my case was of good nature, for the fart came in less time than usual.

In connection with this, I recollected to my mind an incident:

On 14 of November 1930, the then

Prime Minister Yuko Hamaguchi was shot by an assassin from a pistol at Tokyo Station when he was just going to leave for Kansai District to attend the Grand Military Maneuver held there. The bullet hit him at the abdomen. By virtue of the excellent treatment of Professor Shioda and Manabe of the then Tokyo Imperial University, the wound in the intestines was stitched very well. All Japanese nation, not to speak of the doctors concerned, awaited the sign of renewed vermiculation of the Premier's intestines—a fart from within his body.

Of course, I myself had no direct relation with the wounded statesman. But I remember how anxiously I awaited the fart. At last the nation-wide expectation was satisfied—by a fart! I remember the press reported it under big headlines, though not in a special extra issue.

Who could foresee then, that 22 years later my family should wait for a fart from me just as earnestly as the Japanese people did in anxiety for Premier Hamaguchi?

An old Japanese proverb says, "What is happening on other people today may happen on you tomorrow." I could not help reminding me of these words.

I wish that each reader will not look upon cancer as other people's business, but regard it as an unhappiness which may possibly fall upon himself. I wish everyone to take this into consideration and to take better care of their digestive system.

Now, coming back to the main topic, the fart discharge had been so earnestly waited for by all. On my side I awaited it partly because I knew that fluid diet would be allowed after the fart.

The not unusual complication of intestinal obstruction ensued and

*Excerpts from translation by Fumio Kagawa of a cancer patient's personal-experience report appearing in *Bungei-Shunju*, a leading popular magazine widely read by Japanese intellectuals. Reproduced by permission of the Embassy of Japan, Washington, D. C.

On the 13th day the surgeon did not leave my bedside even for a minute, giving out commands to nurses who were practicing the above treatment. But not a sign of fart was to be seen. At last he asked my wife to come to his room for consultation.

To tell in short about this re-operation, they tore off the obstruction and made a new path to the intestines to prevent another obstruction which might arise in the future. I will not dwell upon my conditions thereafter, because there was little difference from that of the previous operation. Only I awaited the fart much more eagerly than before. At last it came 48 hours after the operation, as is said normal in most cases.

Thus I recovered my health day after day. On the seventeenth day after leav-

ing the hospital, I went to my company, about 20 minutes' walk from my house. Since that day I have been working up to this time. When the election campaign of the Lower House began in September, I was healthy enough to take active part in it to help a friend of mine running as a candidate.

Anyhow, I have learned through this precious experience that one's life depends upon the way he takes care of himself. Laotzu, an ancient Chinese philosopher, said: "Our fortune is not decided by Heaven, but by ourselves." I have now understood with all my heart how true this old teaching is.

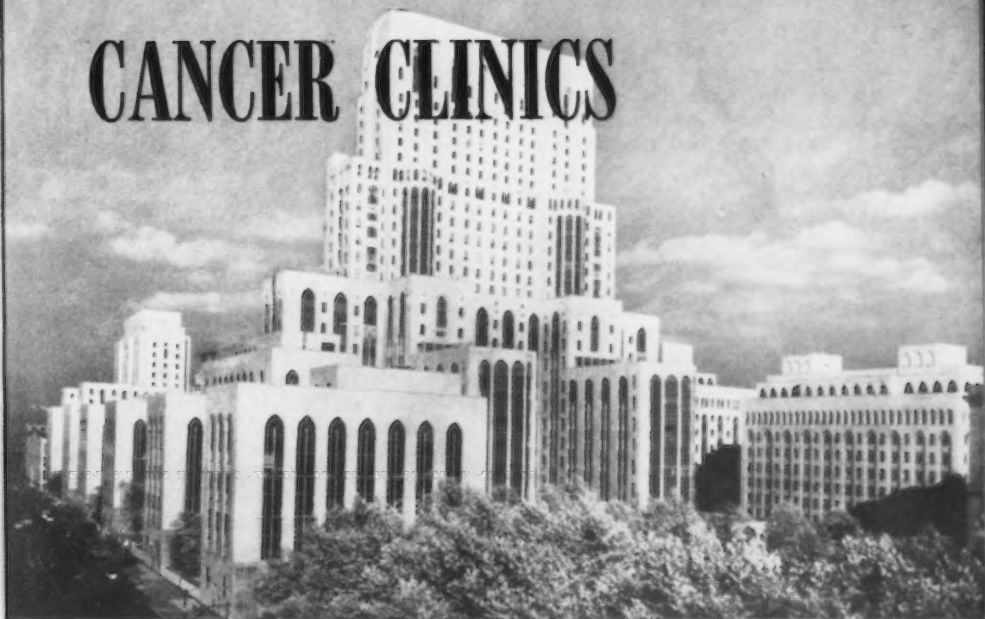
Mr. Nitta is to be congratulated on his intelligent insistence upon early diagnosis and treatment resulting in his restoration to useful citizenship.

In Rectal Bleeding, Think of Cancer First

In cancer of the large intestine, the first symptom may be rectal bleeding or a slight but persistent change in bowel habit. Rectal bleeding from tumors of the descending portion of the large bowel is usually bright red and may be accompanied by mucus, while bleeding from tumors of the other portions may be darker. In tumors of the ascending portion, the change in bowel habit is toward a loose stool, while in tumors of the descending portion, the change is toward constipation. The appearance of hemorrhoids or enlarging hemorrhoids is sometimes the attracting symptom. Occasionally, an unexplained anemia or an attack simulating appendicitis may be the first indication of a tumor of the ascending portion of the large bowel. A digital examination of the rectum should be done methodically. When the upper portion is reached, the patient should be instructed to bear down, as if having a bowel movement, so that the expulsion effort will bring more mucosa within reach of the examining finger. Early rectal cancer is usually felt as a small indurated area. With growth, the tumor becomes an irregular mass. As part of the digital examination, movability of the tumor should be determined.

Goldman, Leonard B.: Fundamentals of Clinical Cancer. New York. Grune & Stratton, Inc., 1953; p. 134.

CANCER CLINICS



MODERATOR: Our clinic today is concerned with certain lesions of the distal colon, and our purpose is to inquire, "What constitutes an adequate examination of this part of the bowel?"

Case 1

RESIDENT: The first patient was a 54-year-old man who began, six months before admission, to have easy fatigue, lack of ambition, belching, and mild diarrhea. There were two to three formed stools daily, with no blood. In the two months before admission, he successively developed low-back pain, pleuritic pain in the right upper quadrant, low-grade fever with night sweats, and a transitory cough. On admission, he was pale, had a temperature of 38°C., widening of the mediastinum, râles at both bases, left pleural effusion, a pericardial friction rub, and an enlarged liver. Rectal examination, with the patient in the knee-chest position, was negative. Hemoglobin was 10.5 gm.; red blood cells, 4.0 million. The serum bili-

rubin was 0.3 and alkaline phosphatase, 42.5.

Repeat rectal examination, with the patient in the supine position, revealed a hard, irregularly nodular mass on the anterior wall of the rectum just above the prostate. Proctoscopy revealed a large fungating tumor at this site, apparently fixed to the adjacent tissues, which, on biopsy, proved to be a carcinoma. Hemorrhoids were also present. The patient was transfused in the hope of being made ready for surgery, but he became increasingly weak and icterus appeared. The liver enlarged rapidly and the pleural effusion filled the right chest. He died on the thirty-seventh day after admission.

STUDENT: Why was the tumor not discovered on the first rectal examination? Were the examiner's fingers too short?

MODERATOR: The first rectal examination was performed with the patient in the knee-chest position, in which the pelvic

From the Department of Medicine, The New York Hospital—Cornell Medical Center, New York, New York.

Written, by invitation, by Thomas P. Almy, M.D.

viscera fall away from the examining finger. With the patient in the left lateral or supine position, and especially if he bears down, high-lying lesions are more likely to be felt. May we have the next case?

Case 2

RESIDENT: This 29-year-old woman had been married for nine years, was childless, and was nervous and easily upset. For eight months, she had had occasional rectal bleeding, in small amounts, after the bowel movement. For three months she had had constipation alternating with diarrhea, together with tenesmus, cramps, and pain in the right lower quadrant. General physical examination was negative. Following a single examination of the stool for parasites, she was treated unsuccessfully for supposed amebiasis. After one month, she was referred to us with a diagnosis of mucous colitis. Digital examination of the rectum was negative. On proctoscopy, however, a bleeding annular tumor was discovered at 15 cm. from the anal margin, which, on biopsy, proved to be a typical adenocarcinoma. Laparotomy one week later revealed the tumor to be inoperable, with liver metastases. Colostomy alone was performed.

MODERATOR: I am sure you realize that youth offers little protection against carcinoma of the colon. This patient's lesion was too high to have been felt by digital examination but could have been found by proctoscopy on her first visit to a physician's office.

VISITING PHYSICIAN: How can you proctoscope a patient who is not prepared?

MODERATOR: The patient can be prepared in five minutes by one of the phosphate-enema preparations (Clyserol or Fleet Enema) given right in the office. Hence, proctoscopy can easily be added to the examination of the patient on his first visit.

STUDENT: Shouldn't a proctoscopy always be done by a specialist? Have not deaths occurred from perforation of the bowel?

MODERATOR: For every man who has

died because he was proctoscoped, a thousand have died because they were *not* proctoscoped *soon enough*.

Case 3

RESIDENT: This 53-year-old housewife began to have streaks of blood on the stool eighteen months before admission, followed six months later by mucus in the stools and slight diarrhea. Ten months before admission, after proctoscopy and barium enema, she was told she had a mild case of ulcerative colitis. Six months later because of progression of symptoms, these procedures were repeated, with the same conclusion. Physical examination revealed a well-nourished woman, not appearing ill. Abdominal and rectal examinations were normal. Proctoscopy to a depth of 18 cm. revealed a normal mucosa with angulation and fixation of the lower sigmoid. Bloody purulent material was seen to come from above. May we see the roentgenograms on this patient?

RADIOLOGIST: Barium enema taken a year ago was read as negative (Fig. 1). Note, however, that the sigmoid loop is



FIGURE 1. Barium enema of patient 3, eight months after the onset of blood in the stool.

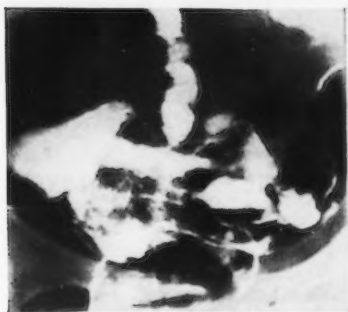


FIGURE 2. Spot film of the sigmoid colon of patient 3, showing annular constricting lesion of the colon.

not clearly seen in profile. No spot films were taken. Also, the bowel is not adequately prepared. When we repeated the studies, we had good preparation, but the standard films did not show any lesion. After careful positioning and spot-film examination, we found this annular lesion of the sigmoid, which is almost certainly a carcinoma (Fig. 2). Has she been operated upon yet?

RESIDENT: Yes, and a carcinoma was found at the site you have indicated. It was resected and an end to end anastomosis performed. It is remarkable, in view of the duration of her symptoms, that there were no metastases in the liver or lymph nodes, no involvement of the serosa, and only partial penetration of the muscular layers of the colon. Her prognosis, therefore, is good.

MODERATOR: At the other extreme, of course, we find patients who, after symptoms of only a week or two have an entirely inoperable lesion. We must realize that there is great variability in the natural history of colon cancer yet do our best to make the diagnosis in each case as early as possible. Here it seems clear that the diagnosis was unduly delayed because the importance of spot-film examination of the sigmoid was not appreciated.

In the final case, let us see HOW EARLY we can make the diagnosis, and whether we can actually PREVENT the development of cancer. . . .

Case 4

RESIDENT: This 56-year-old man was being followed in the clinic for an active duodenal ulcer. Under treatment he was relieved of typical ulcer symptoms but developed "gas pains" and increasing constipation. This might have been due to medication, but for thoroughness a proctoscopy was performed. At 10 cm. from the anus on the anterior wall, an 8-mm. pedunculated polyp was seen. The barium enema was negative. The polyp was wholly removed by biopsy forceps, and pathological section of the entire growth is shown (Fig. 3). You will note that one portion of this is histologically normal mucosa and another portion is a carcinoma.

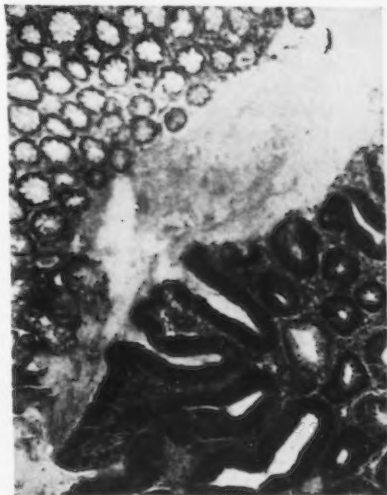


FIGURE 3. Pathological section of an entire polyp of the rectum. On the left is normal mucosa; on the right, a well-developed carcinoma.

MODERATOR: This one section, it seems to me, demonstrates the need for total excision of every polyp. A random bite of the forceps, or incisional biopsy, might have got only normal mucosa and missed the carcinoma entirely.

ATTENDING PHYSICIAN: Should this pa-

tient have an abdominoperineal resection?

MODERATOR: No, the radical operation should be performed only if the malignant cells were seen, on serial sections of the polyp, to invade the basement membrane or the stalk. Here the diagnosis of carcinoma is based entirely upon the cytological characteristics, without invasiveness, and total excision of the growth itself with the immediately surrounding mucosa is sufficient. The patient should, of course, be proctoscoped again after one or two months, to be sure the tumor has not grown back, and as a further check on the presence of additional polyps not previously discovered.

STUDENT: Should every rectal or sigmoid polyp be excised?

MODERATOR: Yes, because evidence indicates that at least 5 per cent of them are carcinomas.

RESIDENT: Can any physician remove them, or should they all be turned over to a surgeon?

MODERATOR: We feel that excision by the biopsy forceps of a small polyp lying below the level of the peritoneal reflection (or about 10 cm. from the anus) can be safely carried out by any careful physician. Even under these conditions, an occasional case may bleed severely. With lesions larger than 1 cm., those on long stalks, or those above the peritoneal reflection, danger from hemorrhage or perforation is more significant, and the excision should be done by a surgeon.

Articles published previously in CA relating to neoplasms of the large bowel:

What the Nonspecialist Should Know about Cancer of the Rectum. 1:79, March, 1951.

Rehabilitation after Colostomy. 1:161, July, 1951.

Proctosigmoidoscopy: Its Technique. 1:189, Sept., 1951.

Odor Control for Wet-Colostomy and Ileostomy Patients. 4:27, Jan., 1954.

Numerous abstracts: See annual indexes under Colon, Rectum, and Sigmoid.



DOCTORS DILEMMAS

Q *Considerable difference of opinion exists among our surgical and gynecological staff on the soundest treatment of cervical "carcinoma in situ." The literature appears to be somewhat less than unanimous in its recommendations. Can the matter be more clearly delineated at present?*

A Without question the treatment of the earliest recognized form of cervical cancer is associated with even more varied opinions than those offered in connection with the more advanced stages of the same disease. The most important first step is of course accurate diagnosis. The term "in situ" excludes any degree of invasion, with the possible exception of cervical gland involvement. A single biopsy indicating "in situ" disease may miss areas of the cervix that show definite invasion. Repeat, generous biopsies of the quadrant type or those achieved through scalpel coning or tracheloplasty are required to establish a diagnosis of "in situ" carcinoma firmly. Once this has been done, therapy can be approached intelligently on the basis of the age and gynecological status of the patient. The consensus of the most experienced is that, when an "in situ" cancer has been accurately diagnosed, the emergency action so frequently associated with the prompt treatment of other types of cancer is not imperative and sufficient time can be taken to evaluate the gynecological status of the patient carefully and to continue study and follow-up. In general, conservative surgical treatment, par-

ticularly in the younger patient in whom the condition is not uncommonly diagnosed, is sound. Radiation and even total hysterectomies in this group are unjustified without evidence of disease beyond the limits of true "in situ" carcinoma.

Q *My patient, 36 years old, was operated on for cancer of the breast three years ago. Eight months ago she showed up with widespread metastatic disease and in extremely poor general condition. However, without any medication (other than sedation and analgesics) she suddenly began to improve and there is now a suggestion of healing in some of the bone metastases and diminution in the amount of pain. What is the explanation for something like this?*

A It is possible that this patient had metastases to both ovaries and that the function of the ovaries was destroyed by the tumor itself. Were the patient somewhat older it would be possible that intervening physiological changes in steroid metabolism incident to the climacteric might be responsible for or contribute to the apparent change in the growth rate of the tumor. The improvement in your patient will probably be only transitory; hence the use of androgenic hormones or castration should certainly be considered as a form of therapy. Present-day studies of the effect of adrenalectomy and even hypophysectomy for these patients are still too new to warrant definite conclusions as

to the degree of benefit to be expected from such procedures.

Q *During the past six months I have had three patients with terminal cancer who developed paraplegia of the lower extremities and, at present, I have a patient with a lymphosarcoma who is developing cord symptoms. Roentgenograms of the spine are entirely normal. Is it possible to prevent or ameliorate the progression of symptoms?*

A The lymphomas frequently invade the meninges and spinal cord without associated bone involvement, giving rise to both nerve-root and spinal-cord symptoms. If it is at all possible to localize the level of the process, radiation often results in dramatic improvement. If you are unable to localize the lesion clinically or by myelography, radiation can be given over a liberal portion of the spine if necessary. The administration of nitrogen mustard is sometimes equally effective in controlling this complication. Although the lymphomas respond much better to radiation therapy and chemotherapy than do other forms of cancer, significant improvement is often noted following radiation and/or HN2 in patients with lung and breast cancer. Surgical decompression is sometimes effective in the management of cord metastases owing to cancer but is ineffective in treatment of this complication of the lymphomas.

Q *I have a patient with an old radio-dermatitis of the face. He has had a few skin cancers that have been easily taken care of. He believes that his face is being*

made worse by exposure to his television set. He has been told and believes that small amounts of roentgen rays are produced in the television tube. I would appreciate whatever information you can give me.

A Expert opinion holds that there are no radiation hazards with the conventional type of TV picture tube as used on the home set and when operated at its normal voltage. Under extraordinary circumstances, such as factory testing and abnormal field operations, the voltage of the tubes may be high, in which case the emission of roentgen rays is not insignificant. However, when the tube voltage is excessively high, the image is not satisfactory and prolonged viewing is therefore unlikely. It appears then that there is no connection between your patient's radio-dermatitis and his viewing television.

Q *A patient with chronic leukemia for the past three years feels perfectly well despite the fact that his hemoglobin level is about 9 gm. He has had transfusions on several occasions but within a week or two the hemoglobin falls to the previous level. How vigorous should I be in trying to restore more normal hemoglobin and red-cell levels?*

A Many of these patients feel well and do well providing hemoglobin does not fall below 8 gm. It is almost always difficult if not impossible to bring hemoglobin levels to normal in these people. Several investigators report that drastic attempts to raise hemoglobin by transfusions are not only unsuccessful but result in hemolysis.

It is a miscarriage of not only trust, but integrity as well, for the surgeons to submit a patient to surgery without first discussing the possibility of the establishment of a permanent colostomy.

Bacon, Harry E.: *Anus, Rectum, Sigmoid Colon*, 3 ed. Philadelphia. J. B. Lippincott Co., 1949.



new developments in cancer

Carcinogen Binding . . .

Wiest and Heidelberger (Univ. of Wisconsin) have forged another link in the chain of evidence beginning to indicate how carcinogens act. They administered a radioactive hydrocarbon (1,2,5,6-dibenzanthracene-9,10- C^{14}) to mice of several strains. Then after varying periods they examined the affected tissues and determined where the hydrocarbon or its metabolites lodged. In one set of experiments the carcinogen was painted on the shaved backs of the mice. They found the radioactive fraction irreversibly bound to nucleoproteins and to particulate and soluble proteins but not to nucleic acids. In another series of tests the hydrocarbon solutions were injected into the submaxillary gland. The investigators found protein-bound radioactivity in gland-cell fractions—again with nucleoprotein but no nucleic acids.

Tell the Patient? . . .

Ravdin and Fitts (Univ. of Pennsylvania) have polled Philadelphia's physicians as to their custom of telling the patient he has cancer. Seventy per cent never tell or usually do not tell. These physicians were largely made up of radiotherapists and others who treat the silent tumors,

most of them incurable. Thirty per cent always or usually tell. And these were mainly dermatologists who treat lesions that are easily detectable and frequently curable. The questionnaires came back with strong voluntary statements by proponents and opponents of the idea of telling. One attributed the urge to tell in some cases to sadism. Another declared that most patients knew, from the type of treatment given them, that they had cancer and that it was cruel to send them to their deaths burdened by knowledge of the deception.

Leukemia . . .

A strain of mice (C3H) with a normal 95 per cent mammary carcinoma has suddenly developed leukemia. Figge (Univ. of Maryland) reports that 70 per cent of the animals, male and female, now show leukemia—possibly as a result of a mutation. Maryland investigators are attempting to determine whether a new virus has appeared in the strain or whether the milk factor has been altered in some way.

Physics of Genetics . . .

At several centers biologists are reporting that such physical factors as light, heat, and pressure exert important in-

fluences on biological reactions, including mutation rates. Climate, altitude, and even the time of day may influence results—accounting for differences in experimental results.

Teratomas . . .

Fekete (Jackson Memorial Laboratory) is experimenting with teratomas—tumors sometimes occurring in the ovary, testicle, or more rarely elsewhere in the body. They frequently contain highly specialized tissues—such as nerve, cartilage, bone, and muscle—along with the completely unspecialized tumor tissue. The unspecialized cells do virtually all the growing in these tumors. One of the teratomas—composed largely of specialized cells—was confined to one ovary. Another—predominantly of unspecialized cells—spread widely from the ovary throughout the body cavity. A third one, recently found, was located in the mouse's neck rather than in the ovary. Stevens has observed seventeen testicular teratomas in an inbred strain of mice. Some occurred in young mice and possibly existed even before the animals were born. Usually they did not enlarge the testis; one grew rapidly when transplanted to other mice.

Resistance to Tumors . . .

Kaliss (Bar Harbor) has succeeded in overcoming mouse resistance to a homograft—a tumor that occurs in other mice of the same strain. He did it by injecting into the mice before transplantation: (1) normal tissues, (2) killed cancer tissue, or (3) antisera to these tissues taken from other animals of the same strain. Apparently, the host is changed by the injections of the tissues prior to grafting. The graft may also be changed by its sojourn in a "foreign" host. The change in the graft is indicated by the ability to survive in untreated hosts of several different inbred strains of mice.

Day and Snell are studying the biochemistry of resistance to tumor transplants. Since this resistance can be broken down in some hosts by injections of certain spe-

cific tissues from other strains of mice, the possibility of characterizing this resistance is good.

Borges is interested in the role of the reticulo-endothelial system (spleen, lymphatics and other antibody-producing organs) in knocking out cancers. He has surgically joined mice resistant and susceptible to a transplanted tumor. The two share a common bloodstream. Do antibodies in the resistant mouse destroy the tumor in the susceptible host? No—not so far, at least.

Stomach Balloons . . .

The technique of having patients with suspect stomachs swallow an abrasive deflated balloon has been tested by Chapman, Klopp, and Platt (George Washington Univ.). The net-covered balloon is inflated in the stomach, deflated, and withdrawn. Stomach contents clinging to it are then examined microscopically for the presence of cancer cells. The Washington investigators advised seventy-one persons with digestive complaints but no known stomach cancers to take the test, the nature of which was not disclosed until it was given. Only six patients did not report for the sight-unseen experience. Of the sixty-five patients who showed up for the test, four declined to undergo it after it was explained; nine started it and gave up without completing the test; seven tried it, some twice, but couldn't swallow the balloon. Fifty specimens were collected from the forty-five patients who completed the test. (Six were called to repeat the test, but only five chose to return.) It took an hour or two to give each test and up to several hours more to process and study the slides of each patient. Then the patients were given an upper-gastrointestinal series by the radiologist (total time: ten to twenty-five minutes). The balloon technique produced one false negative and one false positive. The investigators concluded that the test (1) produces highly satisfactory cytological specimens, (2) is not readily accepted by patients, and (3) is prohibitively time-consuming for routine detection.

cancer -- an influence widely recognized as inherited. He is studying, in animals ranging from mature to senescent, the genetic regulation of pituitary production of ovary-stimulating hormone and the genetic capability of the ovary to produce sex hormones. The observations will be correlated with incidence of tumors in inbred mice.

Russell is tracing the effect of certain bad genes -- lethal and deleterious -- on mice from the womb to the tomb to learn ways in which genes act on growth and differentiation. These genes (W, W', and w) lead to such diverse symptoms as severe anemia, sterility, and lack of pigment in the fur. Finding what lies behind each lesion, and how they are interrelated, may give evidence of the basic action of the genes. Russell and other investigators have shown that the anemia involves delay in forming protoporphyrin, one part of the hemoglobin molecule. The sterility, caused by germ-cell failure, is produced independently of the anemia. Russell does not know yet how the pigment peculiarities are related either to germ cell or to blood phenomena.

Sawin, in rabbit studies, is exploring the influence of genes upon normal and abnormal growth and specialization of cells and tissues as compared with abnormal processes that bring prenatal death, arrested growth, and monstrous development; fertility or sterility; long and vigorous life or early senescence; and susceptibility to various diseases, including cancer. He has devised a system of measuring tissues and organs as standards of embryonic development, childhood growth, maturity, and old age. He has found that ovarian function, much more than the pituitary, governs the mother rabbit's ability to lactate and accounts for prenatal death of offspring.

Murray is attempting to supply scientists in many centers here and abroad with animals tailor-made for specific research problems. Breeding experiments have produced strains that reflect many of the genetic defects found in humans, as well as other psychological and physiological pathology. More than four hundred institutions have received Bar Harbor animals since 1948. More than 156,000 mice representing sixty strains have been shipped out in seven months. Thanks to enormous data compiled, every animal has a predictable future -- the size it will attain, the diseases it will come down with, the time and cause of death.

White and Reinert are investigating the great tumors that are found on spruce trees on Mt. Desert Island.

They do not know the cause of the tumors. Clues include: tumors are limited to trees close to the salt water, especially on exposed headlands; they originate in single cells near the pith of very young twigs.

White and Waymouth have grown cultured mouse cancers in test tubes supplied with chemically defined media -- brewed from the contents of bottles from the chemist's shelf. The cells of one tumor, which are still growing rapidly, have all been supplied with the synthetic medium for at least ninety days -- but not ninety consecutive days. They were periodically on and off the defined diet. The concentration and kinds of sugar and the bicarbonate in the synthetic diet have proved to be surprisingly important -- in some respects more so than modifying amino acids, vitamins, and other complex essentials.

Snell is studying immunogenetics using tumors as a tool -- the ability of some hosts to accept tumor transplants and grow them, and the resistance of other hosts to transplants. This basic study involves principles of immunity, since tumors arising in a certain strain carry with them the immunity-conferring substances (i.e., antigens) characteristic of that strain. These tumors are accepted best by those hosts of other strains in which blood types, for instance, are most like the tumors' mother (i.e., indigenous) strain. (Note: there is not the slightest possibility stemming from this work of developing an antiserum against spontaneous tumors.)

COMING MEDICAL MEETINGS

Date 1954	Association	City	Place
May 17-19	American College of Surgeons (Sectional)	London	
May 20-22	American Gynecological Society	Hot Springs, Va.	
May 31- June 3	American Urological Association	New York City	Waldorf-Astoria
June 2-5	American Proctologic Association	Los Angeles	
June 17-20	American College of Chest Physicians	San Francisco	
June 18-22	Canadian Medical Association	Vancouver, B. C.	
June 21-25	American Medical Association	San Francisco	
July 23-29	Sixth International Cancer Conference	São Paulo, Brazil	
July 26-29	International Congress of Obstetrics and Gynecology	Geneva	
Aug. 9-13	National Medical Association	Washington	
Aug. 14-21	International Congress on Mental Health	Toronto, Ontario	University of Toronto
Sept. 2-9	International Society of Cell Biology	Serster, Netherlands	
Sept. 6-10	International Congress of Geographic Pathology	Washington	
Sept. 7-10	International College of Surgeons	Chicago	
Sept. 12-14	New Hampshire Medical Society	Bretton Woods	
Sept. 12-14	Vermont Medical Society	Bretton Woods	
Nov. 30- Dec. 3	American Medical Association, Clinical Session	Miami	

SAVE & PROTECT

Your issues of CA with

"BIND-ALL"

magazine binder

IMITATION LEATHER MAGAZINE
BINDER THAT HOLDS
2 YEARS ISSUES.

YEAR & TITLE STAMPED
IN GOLD ON BACKBONE.

JOURNAL CAN BE INSERTED
AND REMOVED WITH NO EFFORT.

Price per binder \$2.25



BINDER WITH 1 ISSUE ➡

BINDER WITH 2 YEARS ISSUES ➡

COUPON

Sendor Bindery, Inc.
129 Lafayette Street
New York 13, N. Y.

Enclosed please find check or money order of \$ _____

for _____ "BIND-ALL" binders. Year _____

Name _____

Address _____

